INTERNATIONAL RECORD OF MEDICINE

VOLUME 170 NO. 7 | JULY 1957

ORIGINALLY PUBLISHED AS AMERICAN MEDICAL INTELLIGENCER, FOUNDED PHILADELPHIA, 1837

SYMPOSIUM ON MEDICAL AND PSYCHOLOGICAL ASPECTS OF FOOD AND COOKING. PART II.

Special Problems of Food and Cooking Today: Psychiatry
WINFRED OVERHOLSER AND ARLEEN G. HAVSGAARD

Science and the Art of Cooking — J. W. BROWN

Some Nutritional and Therapeutic Aspects of Wine and Cognac — HAROLD H. LEVY

Chlorpromazine as an Adjunct in Managing Tuberculous Patients — HARRY SHUBIN, CHARLES A. HEIKEN, ALLEN GLASKIN, EDWARD PENNES, AND J. ARSENIAN

MEDICAL INSTRUMENTS SECTION:
The Role of Electrophoresis in Medicine — MIRIAM REINER

INTERNATIONAL CLINICAL NEWSLETTER

BOOK REVIEWS

ADVANCED REPORTS FROM CURRENT MEDICAL MEETINGS

A JOURNAL OF MD PUBLICATIONS, INC.

MD INTERNATIONAL SYMPOSIA MONOGRAPH No. 3

Psychiatry *and* Religion

Thirteen scientific authorities and ministers of different religions explore the conflicts of the human psyche and open up new vistas for meaningful cooperation between the psychiatrist and churchman. An absorbing discussion of interest to the psychologist, sociologist, anthropologist, psychiatrist, theologian, religious historian, the clergy, and the intelligent layman. A most unusual and attractively bound volume. 68 pp. **Price: $3.00.**

C O N T E N T S

SYMPOSIUM ON PSYCHIATRY AND RELIGION
An Introduction by Werner Wolff, Ph.D., Professor of Psychology, Bard College, Annandale-on-Hudson, N. Y.

THE PSYCHE AND THE SYMBOLS OF RELIGION
by M. Esther Harding, M.D., M.R.C.P., New York City.

PSYCHOANALYSIS AND RELIGION, AN HISTORICAL VIEW OF FREUD
by Fred H. Blum, Dept. of General Studies, Social Science Program, University of Minnesota, Minneapolis, Minn.

A CURRENT PSYCHOANALYTIC CONCEPT OF GOD
by Josephine H. Ross, Ph.D., New York City.

ANTHROPOLOGIC VIEW OF A PRIMITIVE RELIGION
by Gladys A. Reichard, Professor of Anthropology, Barnard College, Columbia University, New York City.

THE SOCIOLOGIC DEFINITION OF RELIGION
by Joseph Maier, Ph.D., M.A., Newark College of Arts and Sciences, Rutgers University, New Brunswick, N. J.

TOWARDS AN OPERATIONAL DEFINITION OF RELIGION
by Rabbi Samuel Glasner, Ed.D., Director, Dept. of Reform Jewish Education, Board of Jewish Education, Baltimore, Md.

RELIGION AND PSYCHOTHERAPY: PRACTICAL ASPECTS
by Lawson G. Lowrey, M.D., A.M., Asst. Clinical Professor, College of Physicians and Surgeons, Columbia University; Associate in Psychiatry, Vanderbilt Clinic, New York City.

VALUE SYSTEMS IN THE PSYCHOTHERAPEUTIC PROCESS
by Warner L. Lowe, Ph.D., Asst. Director, Alfred Adler Mental Hygiene Clinic, New York City.

PERSONALITY NEEDS, RELIGION, AND PSYCHOTHERAPY
by Alexander A. Schneiders, Ph.D., Professor of Psychology and Director of Psychological Services, Fordham University, New York City.

PSYCHOTHERAPY AND THE MINISTRY
by Abraham N. Franzblau, M.D., Ph.D., Professor of Pastoral Psychiatry and Dean of New York Schools, Hebrew Union College, Jewish Institute of Religion; Asst. Attending Psychiatrist, Mount Sinai Hospital, New York City.

THE NEED TO BELIEVE
by Mortimer Ostow, M.D., New York City.

SPECIAL EDITORIAL:
On Christmas and Neuroses
by Félix Martí-Ibáñez, M.D.

WRITE TO: MD PUBLICATIONS, INC., 30 EAST 60TH STREET, NEW YORK 22, N. Y.

INTERNATIONAL RECORD OF MEDICINE

ORIGINALLY PUBLISHED AS AMERICAN MEDICAL INTELLIGENCER, FOUNDED PHILADELPHIA, 1837

A JOURNAL OF ADVANCED EXPERIMENTAL AND CLINICAL REPORTS

FELIX MARTI-IBAÑEZ, M.D., Editor-in-Chief
Professor and Director of the Department of the History of Medicine,
New York Medical College, Flower and Fifth Avenue Hospitals, New York, N. Y.

VOL. 170 NO. 7 *WHOLE NUMBER 2893* *JULY 1957*

The *International Record of Medicine* is published monthly by MD Publications, Inc. (30 E. 60th Street, New York, N. Y., Félix Martí-Ibáñez, M.D., President). ©Copyright 1957 by MD Publications, Inc. Entered as second class matter at the Post Office, Washington, D. C., under the Act of March 3, 1879. Matter appearing in *International Record of Medicine* is covered by copyright. The reproduction of articles (or parts of articles) appearing in *International Record of Medicine* is not permitted. Permission must be received in writing from the editor for reprinting material in whole or in part. Subscription Rate: $11.00 for one year, $28.00 for three years.

INTERNATIONAL RECORD OF MEDICINE

INSTRUCTIONS TO CONTRIBUTORS

All manuscripts submitted for publication in INTERNATIONAL RECORD OF MEDICINE should be sent to Doctor Félix Martí-Ibáñez, MD Publications, 30 East 60th St., New York 22, N. Y. Manuscripts should not include data published previously and it is understood that any manuscript submitted is not being submitted elsewhere.

Manuscripts—All manuscripts should be typewritten, double spaced, and on only one side of paper 8½ by 11 inches. They should be mailed in a flat package. *The original and one carbon copy of the article are required.* Original drawings or tracings should not be sent. Glossy photographs, no larger than the manuscript paper, of all illustrations should accompany the copies of the manuscript. Prints should be sufficiently clear to permit the making of engraver's cuts without retouching and to allow reduction to approximately one-third size.

Tables, figures, charts, etc., must be typewritten on separate sheets and should be placed in proper sequence in the manuscript. Footnotes should not be included in the text pages. All references are to be numbered consecutively and typed on a separate sheet. Numerals are used for figures for all definite weights, measurements, percentages, and degrees of temperatures. All indefinite and approximate periods of time and other numerals which are used in a general manner should be spelled out. Standard abbreviations should be used whenever weights and measurements are given in the metric system. The forms to be used are: Gm., ml., Kg., mg., μg., mm., and l. Per cent should be written out in the text.

Footnotes and Bibliographies should conform to the style of the Quarterly Cumulative Index Medicus published by the American Medical Association. This requires, in the order given, last name of author, initials, title of article in the language in which it was written, name of journal with accepted abbreviation, volume number, page number, and year.

Illustrations.—A reasonable number of half-tone illustrations will be reproduced free of cost to the author but special arrangements must be made with the editor for color plates, elaborate tables, or extra illustrations. Pen drawings and charts should be drawn and lettered only in India ink or black typewritter ribbon (when the typewriter is used). Only good photographic prints or drawings should be supplied for half-tone work. All photographs submitted should be numbered and bear on the back author's name, address, and title of article. Top of picture should be indicated.

Reprints.—Authors will be sent an estimate of the cost of reprints with galley proofs. Reprints may be ordered anytime after manuscript has been set in type but not later than 30 days after the journal has been published.

Business Communications.—All communications in regard to advertising, subscription, change of address, etc., should be addressed to MD Publications, Inc., 30 East 60th Street, New York 22, N. Y. The publisher should be advised of a change in the subscriber's address about 15 days before the date of the issue of the journal with both new and old addresses given.

Subscription Rates.—In the United States and other countries in the United States postal zone—$11.00; single copies, $1.20. In Canada and other foreign countries—$12.00; single copies, $1.40. Remittance for subscriptions should be made by check, draft, post office or express money order, or registered letter payable to MD Publications, Inc.

EDITORIAL BOARD

FELIX MARTI-IBAÑEZ, M.D., Editor

NATIONAL EDITORIAL BOARD

FRED L. ADAIR, M.D., *University of Chicago*

HARRY L. ARNOLD, JR., M.D., *Editor, Hawaii Medical Journal, Honolulu, Hawaii*

W. WAYNE BABCOCK, M.D., *Temple University*

HOWARD C. BALLENGER, M.D., *Northwestern University*

CONRAD BERENS, M.D., *The Ophthalmological Foundation*

ALEXANDER W. BLAIN, M.D., *Wayne University*

ALFRED BLALOCK, M.D., *Johns Hopkins University*

W. F. BRAASCH, M.D., *Mayo Clinic*

ROBERT H. BROH-KAHN, M.D., *New York, N. Y.*

MORTON S. BRYER, M.D., *The Mount Sinai Hospital*

LEROY A. CALKINS, M.D., *University of Kansas*

NORTON CANFIELD, M.D., *New Haven, Conn.*

BAYARD CARTER, M.D., *Duke University*

RUSSELL L. CECIL, M.D., *Cornell University*

F. CO TUI, M.D., *Creedmoor Institute*

FREDERICK A. COLLER, M.D., *University of Michigan*

WILLARD R. COOKE, M.D., *University of Texas*

WALTER T. DANNREUTHER, M.D., *New York University*

CLYDE L. DEMING, M.D., *Yale University School of Medicine*

R. S. DINSMORE, M.D., *Cleveland Clinic*

HENRY DOLGER, M.D., *New York, N. Y.*

I. E. DRABKIN, PH.D., *The College of the City of New York*

DANIEL C. ELKIN, M.D., *Emory University*

LUDWIG A. EMGE, M.D., *Stanford University*

HAROLD K. FABER, M.D., *Stanford University Hospital*

HARRY A. FELDMAN, M.D., *State University of New York*

JOSEPH H. FOBES, M.D., *New York Medical College*

A. STONE FREEDBERG, M.D., *Harvard Medical School, Boston, Mass.*

WILLIS D. GATCH, M.D., *University of Indiana*

LOUIS J. GELBER, M.D., *Rockville Center, L. I., N. Y.*

DAVID GROB, M.D., *Johns Hopkins Medical School*

BERNARD J. HANLEY, M.D., *University of Southern California*

FRENCH K. HANSEL, M.D., *Washington University*

CLYDE A. HEATLY, M.D., *University of Rochester*

HENRY F. HELMHOLTZ, M.D., *Mayo Clinic*

FRANK HINMAN, M.D., *University of California*

CLARENCE B. INGRAHAM, M.D., *University of Colorado*

J. BAY JACOBS, M.D., *Georgetown University*

ROBERT W. KEETON, M.D., *University of Illinois*

HARRY H. KERR, M.D., *George Washington University*

WILLIAM J. KERR, M.D., *Blue Lake, California*

I. NEWTON KUGELMASS, M.D., *New York, N. Y.*

THEODORE LIDZ, M.D., *Yale University School of Medicine*

DEAN M. LIERLE, M.D., *University of Iowa*

IRVINE MCQUARRIE, M.D., *University of Minnesota*

RALPH H. MAJOR, M.D., *University of Kansas*

ALTON OCHSNER, M.D., *Tulane University*

HENRY BOYLAN ORTON, M.D., *Newark, N. J.*

WINFRED OVERHOLSER, M.D., *George Washington University*

JAMES E. PAULLIN, M.D., *Emory University*

FRANKLIN L. PAYNE, M.D., *University of Pennsylvania*

E. D. PLASS, M.D., *University of Iowa*

TRACY J. PUTNAM, *Beverly Hills, California*

B. O. RAULSTON, M.D., *University of Southern California*

LYMAN G. RICHARDS, M.D., *Massachusetts Institute of Technology*

LEONARD G. ROWNTREE, M.D., *Miami, Fla.*

RAYMOND R. SACKLER, M.D., *New York, N. Y.*

MILTON S. SACKS, M.D., *University of Maryland School of Medicine*

MORRIS SCHAEFFER, M.D., *Director, Communicable Disease Center, Montgomery, Ala.*

LEWIS C. SCHEFFEY, M.D., *Jefferson Medical College*

SIDNEY SCHERLIS, M.D., *University of Maryland School of Medicine*

EDWARD A. SCHUMANN, M.D., *Phila., Pa.*

CYRUS C. STURGIS, M.D., *University of Michigan*

HERBERT THOMS, M.D., *Yale University*

DONALD V. TRUEBLOOD, M.D., *Seattle, Wash.*

JAMES J. WARING, M.D., *University of Colorado*

KARL M. WILSON, M.D., *University of Rochester*

FRED W. WITTICH, M.D., *Minneapolis, Minn.*

FLETCHER D. WOODWARD, M.D., *Charlottesville, Va.*

INTERNATIONAL EDITORIAL BOARD

ROMA AMYOT, M.D., *Editor-in-Chief, L'Union Medicale du Canada*

GASTON BACHELARD, M.D., *Directeur de l'Institut d'Histoire des Sciences, La Sorbonne, Paris, France*

GEOFFRY H. BATEMAN, *London, England*

PAUL DIEPGEN, M.D., *Director of Medizinhistorischen Institutes der Johannes Gutenberg Univ., Mainz, Germany*

PEDRO LAIN ENTRALGO, M.D., *Profesor de Historia de la Medicina, Madrid, Spain*

PROF. A. GIGON, *Schweizerische Akademie der Medizinischen, Wissenschaften, Basel, Switzerland*

EDV. GOTFREDSEN, M.D., *Director of the Universitetets Medicinsk-Historiske Museum, Copenhagen, Denmark*

DOUGLAS GUTHRIE, M.D., *Professor of the History of Medicine, University of Edinburgh, Edinburgh, Scotland*

WILLY HARTNER, M.D., *Johann Wolfgang Goethe Universität, Frankfurt a. M., Germany*

E. HINTZCHE, M.D., *Anatomisches Institut, Bern, Switzerland*

BJØRN IBSEN, M.D., *Chief of the Department of Anaesthesiology, Kommunehospitalet, Copenhagen, Denmark*

JUAN B. LASTRES, M.D., *Profesor de Historia de la Medicina, Universidad de San Marcos, Lima, Peru*

PROF. ADOLF MEYER-ABICH, *Elbchaussee 460, Hamburg-Blankenese, Germany*

ANDRE MOULONGUET, M.D., *Paris, France*

PROF. RODOLFO PÉREZ DE LOS REYES, *Universidad de La Habana, Cuba*

AUGUSTO PI-SUÑER, M.D., *Instituto de Medicina Experimental, Caracas, Venezuela*

ILSE ROSENTHAL-SCHNEIDER, Ph.D., *The University of Sydney, Sydney, Australia*

ANIBAL RUIZ MORENO, M.D., *Profesor de Historia de la Medicina, Buenos Aires, Argentina*

KENNETH F. RUSSELL, M.S., F.R.A.C.S., *Associate Professor of Anatomy, The University of Melbourne, Melbourne, Australia*

TH. H. SCHLICHTING, M.D., *Amsterdam, Holland*

HANS SELYE, M.D., *Université de Montréal, Montreal, Canada*

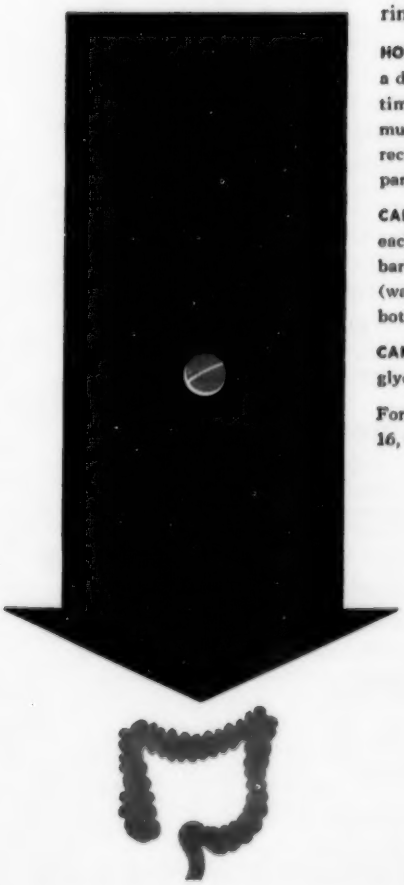
PROF. IVOLINO DA VASCONCELLOS, *President, Sociedad Brasileña de Historia da Medicina Rio de Janeiro, Brazil*

effective, selective therapy

Cantil
for the colon

for functional and organic disorders

CANTIL relieves pain, cramps, bloating...curbs diarrhea...restores normal tone and motility. Selective action focused on the colon avoids widespread interference with normal autonomic function... minimizes urinary retention, mouth dryness, blurring of vision.



HOW CANTIL IS PRESCRIBED One or two tablets three times a day preferably with meals, and one or two tablets at bedtime for patients with ulcerative colitis, irritable colon, mucous colitis, spastic colitis, diverticulitis, diverticulosis, rectospasm, diarrhea following G.I. surgery, bacillary and parasitic disorders.

CANTIL—TWO FORMS CANTIL (plain)—25 mg. of CANTIL in each scored tablet—bottles of 100. CANTIL with Phenobarbital—25 mg. of CANTIL and 16 mg. of phenobarbital (warning: may be habit forming) in each scored tablet—bottles of 100.

CANTIL is the *only* brand of N-methyl-3-piperidyl-diphenylglycolate methobromide.

For more detailed information, request Brochure No. NDA 16, Lakeside Laboratories, Milwaukee 1, Wisconsin.

LAKESIDE

11437

MD INTERNATIONAL SYMPOSIA MONOGRAPH No. 2

MEDICAL WRITING

Good writing is just as essential in the medical profession as in any other field.

In this symposium, a panel of distinguished medical writers describe the how and why of writing clear and cogent medical articles and books.

Invaluable for the physician interested in the practical principles of medical writing, as well as the enrichment of his own culture in the medical humanities.

A very unusual and attractive book gift for a fellow physician.

72 pp. **Price: $3.00.**

contents

THOUGHTS ON THE PHYSICIAN'S WRITING AND READING
by Henry Sigerist, M.D., Pura, Ticino, Switzerland.

HOW NOT TO WRITE A MEDICAL PAPER
by Hans Selye, M.D., Professor and Director, Institut de Médecine et de Chirurgie Expérimentales, Université de Montréal, Canada.

AN EDITOR'S PREJUDICES
by Hugh Clegg, M.D., Editor, British Medical Journal, *London, England.*

MEDICAL WRITING
by Walter C. Alvarez, M.D., former Professor of Medicine, University of Minnesota; Editor, Modern Medicine, *Chicago, Ill.*

BOOKS IN THE PHYSICIAN'S LIFE
by Félix Martí-Ibáñez, M.D., Editor-in-Chief, International Record of Medicine & General Practice Clinics, *New York City.*

WRITE TO: MD PUBLICATIONS, INC., 30 EAST 60TH STREET, NEW YORK 22, N. Y.

INTERNATIONAL RECORD OF MEDICINE

VOL. 170 NO. 7 WHOLE NUMBER 2893 JULY 1957

SYMPOSIUM ON MEDICAL AND PSYCHOLOGICAL ASPECTS OF FOOD AND COOKING. PART II.

WINFRED OVERHOLSER AND ARLEEN G. HAVSGAARD — Special Problems of Food and Cooking Today: Psychiatry — 351

J. W. BROWN — Science and the Art of Cooking — 357

HAROLD H. LEFFT — Some Nutritional and Therapeutic Aspects of Wine and Cognac — 361

INTERNATIONAL CLINICAL NEWSLETTER — opp. p. 368

HARRY SHUBIN, CHARLES A. HEIKEN, ALLEN GLASKIN, EDWARD PENNES, AND J. ABSENIAN — Chlorpromazine as an Adjunct in Managing Tuberculous Patients — 369

MEDICAL INSTRUMENTS SECTION

MIRIAM REINER — The Role of Electrophoresis in Medicine — 374

BOOK REVIEWS

NORMAN JOLLIFFE — Reduce and Stay Reduced — 388

MORRIS FISHBEIN, Editor — Illustrated Medical and Health Encyclopedia — 388

WALTER H. SNELL, AND ESTHER A. DICK — A Glossary of Mycology — 389

ADVANCED REPORTS FROM CURRENT MEDICAL MEETINGS

Case Experiences in Thyroid Disease — 390

The Combined Use of Antibiotic Agents — 391

Neonatal Estrogen Excretion and Its Relation to Postnatal Weight Loss — 391

No Harmless Dose of Radiation — 392

The Possibility of Diagnosis of Early Atherosclerosis — 392

Fluorides and Fluorosis — 393

Arterial Damage and Metabolic Disturbance in Presenile Arteriosclerosis — 393

Rumination: A Psychosomatic Syndrome — 394

Organized Enzyme Systems: Mitochondria — 394

A "Pregnancy" of Five Years' Duration — 395

Progress in the Treatment of Hepatic Coma — 395

Congenital Abnormalities — 396

Use of Analgesic Drugs for Relief of Pain — 396

Significance of the Rheumatoid Factor — 397

Most patients treated with 'Compazine'. . . "showed prompt, marked improvement in their emotional outlook."

Vischer[1] reports that 37 of 38 patients treated with 'Compazine' for psychoneurotic symptoms had "marked" or "moderate" relief. "21 patients were totally free of such symptoms and obtained a better response than to any previous medication. Confusion and depression disappeared dramatically, and primary complaints became less important to them as they became far more relaxed, less nervous and less tense. Many were able to return to work or had renewed interest in their surroundings and hobbies."

1. Vischer, T.J.: Clinical Study of Proclorperazine, A New Tranquilizer for the Treatment of Non-Hospitalized Psychoneurotics, New England J. Med. *256*:26 (Jan. 3) 1957.

Smith, Kline & French Laboratories, Philadelphia

Compazine★

a true tranquilizing agent with minimal side effects

★T.M. Reg. U.S. Pat. Off. for proclorperazine, S.K.F.

INTERNATIONAL RECORD OF MEDICINE

VOL. 170 NO. 7 WHOLE NUMBER 2893 JULY 1957

SYMPOSIUM ON MEDICAL AND PSYCHOLOGICAL ASPECTS OF FOOD AND COOKING. PART II.

Special Problems of Food and Cooking Today: Psychiatry

Winfred Overholser, M.D., Sc.D., L.H.D., and Arleen G. Havsgaard, B.S.†*

SAINT ELIZABETHS HOSPITAL

WASHINGTON, D. C.

There is no considerable evidence today to indicate that the diet of a psychiatric patient should be any different from that of his more fortunate brothers. Stated more succinctly, the psychiatric patient's illness does not, per se, require a different diet. In this respect, institutional feeding of mental patients requires less attention to tailored special diets than does the feeding of the physiologically ill. This, of course, is true only in the light of our present knowledge of the interrelationship of nutrition and mental disorders, and it may be that more significant studies will alter the concept. Special diets, of course, are required in mental institutions for patients who are also physiologically ill. But, as of today, the chief problem confronting the dietitian of a mental hospital is to get the patients to eat the same food that a well adjusted person would select in his own best interest.

It is not enough to put high quality and wisely selected food before the patient. In perhaps a majority of cases, it will be necessary to induce him to eat it. The same considerations apply in stimulating his appetite as in stimulating the appetite of a normal individual. A common misconception, as old as the history of mental illness, is that the disturbed person could not possibly care less what is put before him. It prevails today among untutored hospital employees. As a primary matter, therefore, the dietitian, as an aid in feeding the patient, must first "cure" the employee of this notion. This can be done by training, by seeking to inculcate in the employees a genuine desire to help, by judicious selection of personnel so far as they are available, and, making concessions to the human element, by supervision.

Part I of this Symposium appeared in the May issue.

* Superintendent, Saint Elizabeths Hospital.

† Head Dietitian, Saint Elizabeths Hospital.

FIG. 1. Photograph of patients eating in old dining room at Saint Elizabeths Hospital.

In keeping with the central objective of mental therapy it is even more important that the patient be encouraged to help himself. This accounts for the increasing change-over in mental institutions to a cafeteria type of feeding. The optimum benefit from this type of service results when the patient is permitted some choice in the selection of his food. The majority of patients, when confronted with this type of serving for the first time, will indiscriminately help themselves to everything. If this is permitted, nothing is gained. The patients must be guided, at least for the first few meals, into making a conscious selection. Budgetary limitations will, of course, dictate the amount of the selection permitted. But that, after all, is part and parcel of the dietitian's art, which is to provide wholesome, palatable, and attractive food within the limits of reasonable cost. Such cost may, and most often will, preclude a choice of two different meats for the same meal. But it will not preclude a choice of two vegetables or salads or desserts, or a selection of bread, or of coffee or tea. This may seem a matter of not very great significance. But nothing in mental therapy is a panacea. Any effort that stimulates the patient to adopt a rational form of behavior is worth the making. The aim is to prolong the period of rational behavior until it becomes the pattern of the patient, and forcing a conscious choice on the patient encourages that behavior.

For the same reason the attempt should be made to instill a sense of discipline. This is most easily flouted at breakfast when patients, just rising from bed, can come to the dining room in any style of morning disarray. It is better to awaken the patients earlier and require them to dress and wash before permitting them to eat. This also serves to increase appetite. Further, it has a good effect on most of the patients, who, contrary to current misconception, are not oblivious to what is

attractive in the daily course of living. It requires cooperation of ward nurses, of course, but mental therapy is a team effort.

Just as a patient may be benefited by a well turned out breakfast companion, so may his condition be ameliorated by attractive surroundings. Nowhere is this more important than in the dining room, which is the focal point, or should be, of camaraderie and conviviality in uneventful lives. The effect to be sought is to make it appear that the meals, the product of institutional feeding, are not really being served in an institution. Tables for four are becoming standard fixtures for the new cafeterias of mental hospitals. Conversation is stimulated by smaller seatings. Windows are framed in brightly colored drapes, walls are painted in warm colors, as often as possible, flowers are placed on tables in the cafeterias. The change in therapy is marked, and in retrospect the wonder is that in the drab surroundings that characterized mental hospitals of yesterday, any of the patients made a successful exit.

The institutional effect can be softened by other efforts the dietitian may make. Well received at Saint Elizabeths Hospital is the recent innovation of "brunch" on Sunday morning for those who prefer it to the regular morning breakfast. Ward parties or dances at which ice cream, cake or cookies, and punch or coffee are served are greeted with appealing enthusiasm, seldom equaled in this life by the patients. In the summer months "picnics" are simulated by serving meals out of doors.

The statement made earlier that the psychiatric patient needs no special diet as a consequence of his disorder is no warrant for the dietitian to disregard his eating

FIG. 2. Photograph of new dining room. Note patients helping themselves cafeteria style.

TABLE I

A Week's Menu Served the Patients of Saint Elizabeths Hospital

Date	Breakfast	Dinner	Supper
Sunday	Orange juice Rice Crisp, milk, sugar Scrambled eggs Raisin toast, butter Apple butter Coffee	Pot roast of beef, gravy Mashed potatoes Green beans O'Brien Bread, butter Ice cream, chocolate sauce Hot tea	Vegetable soup, crackers Sliced veal loaf, mustard Baked potato Bread, butter Chilled pear halves Milk
Monday	Stewed prunes Oatmeal, milk, sugar Boiled eggs Cinnamon toast, butter Coffee	Baked smoked shoulder Mustard, mixed pickles Candied sweet potatoes Buttered spinach Bread, butter Baked custard Hot tea	Boston baked beans with bacon strips Perfection salad on lettuce, mayonnaise Hot rolls, butter Chilled applesauce Cookies Milk
Tuesday	Orange quarters Ralston, milk, sugar Grilled bacon Toast, butter, jam Coffee	Swiss steak Buttered noodles Lettuce hearts, French dressing Bread, butter Butterscotch meringue pudding Hot tea	Assorted cold meat and cheese Fried potatoes Buttered peas Graham bread, butter Chilled peach halves Milk
Wednesday	Banana Grapenut Flakes Milk, sugar Fried eggs Toast, butter, marmalade Coffee	Roast veal, gravy Oven-browned potatoes Stewed tomatoes Bread, butter Baked apple with raisins Hot tea	Hamburger patties, catsup, mustard, pickle relish Carrot sticks Escalloped potatoes Hot rolls, butter Cherry pie Milk
Thursday	Blended fruit juice Wheatoata, milk, sugar Baked sausage links Toast, butter, jam Coffee	Roast chicken, dressing, giblet gravy Whipped potatoes Buttered broccoli spears Bread, butter Chocolate chip ice cream Hot tea	Beef stew with vegetables Cottage cheese salad on lettuce, mayonnaise Hot rolls, butter Apricot crisp Milk
Friday	Kadota figs Farina, milk, sugar Scrambled eggs Hot cinnamon doughnuts Toast, butter, marmalade Coffee	Cream of potato soup, crackers Fried fish, lemon wedge Tomato and lettuce salad, mayonnaise Cornbread, bread, butter Pineapple slices Hot tea	Baked macaroni and cheese Harvard beets Hot rolls, butter Crackers, peanut butter Fruit Jello with whipped topping Milk

Table I Continued on page 355

TABLE I (*Continued*)

A Week's Menu Served the Patients at Saint Elizabeths Hospital

Date	Breakfast	Dinner	Supper
Saturday	Grapefruit half Cornflakes, milk, sugar Hot cakes, syrup Toast, butter Coffee	Roast pork, gravy Buttered black-eyed peas Buttered greens Celery sticks Bread, butter Frosted white cake Hot tea	Vegetable soup, crackers Egg salad on lettuce Baked sweet potato Bread, butter Chilled strawberries Milk

habits. These she must attempt to correct. She must recognize that overeating may be a manifestation of lack of a satisfactory parent-child relationship or that a refusal to eat may result as self-punishment for guilt feelings. Nevertheless, her concern must be that each of her charges consumes the amount of food physiologically necessary. This is important, not only for the more obvious reason of the good effect of physical health on the mental condition of the patient, but because there is reason to believe that nutritional deficiencies may be the cause of symptoms of the patient. If symptoms due solely to such deficiencies are eliminated, readier diagnosis of the more significant part of the patient's mental disorder can be made. This necessitates sparing diets for the obese and constant encouragement for those who, for whatever reason, would otherwise go undernourished. There is a tendency, resulting from the press of business, to continue the feeding of special diets when the need for them has ceased. This tendency can be corrected only by adequate observation of the patient. Observation will also permit the dietitian to suit her instructions to the personality of the patient, thus ensuring that he gets the most good from them. It will also help her to distinguish between the deeper neurotic conflicts about food that necessitate special handling and the significantly greater number of phobias about food that can be resolved by a discerning approach. Habits are hard to change, especially food habits, and even in the case of people passing in all respects as "normal." New foods should therefore be introduced a little at a time and with due regard for a propitious moment. Attempts to bully the patient into trying them will always fail. Painfully slow it may be, but the patient must be educated to them. The success of the dietitian is indicated not by the written menu, but by the empty plates. Table I shows a week's menu served the patients of Saint Elizabeths Hospital. This menu was picked at random and represents, we think, considerable variety within the limits of reasonable cost.

Geriatric patients present special problems. It is necessary to include bulk foods in their diet as well as foods with a laxative effect, since the peristaltic ability of the colon diminishes with the years. Foods must be chopped in most cases for easier digestibility. Lettuce should be shredded fine and cooked vegetables should be chopped after cooking, rather than before, to preserve vitamins. They are tastier than puréed vegetables and more attractive. These patients have to be observed while eating as some are afraid to have it appear that they are unable to masticate

their foods and, in the absence of observation, their physical condition would soon degenerate, thus necessitating the added labor of special diets. Care should be taken that geriatric patients drink sufficient fluids at mealtimes since many of them, when they return to the wards, find the effort of resorting to the ward drinking fountain too tiring.

A force exerting a good effect on the eating habits of patients in mental hospitals in particular are the new "wonder" drugs, e.g., chlorpromazine and reserpine. These drugs are no cure in themselves for psychoses or neuroses. Their good effect lies in their capacity to improve the emotional tone of the patient. The drug relaxes the patient and seems to stimulate the appetite; hence, the patient tends to eat more. Nine women to whom chlorpromazine was administered for a 15 week period at Saint Elizabeths registered a median weight gain of 16 pounds. The older drugs, liver extract and insulin, are also given to stimulate appetite.

The dietitian in a mental hospital will not have to devote so much of her time to the preparation of special diets as would the dietitian of a general hospital. The time thus saved her can be spent in close observation of, and consequent attention to, the individual needs of the patients. There should be opportunity to do so. Lamentably enough, some of them will be around for a long time.

This indicates the necessity of constant stimulation of the appetites of mental patients. The same requirement is not present when we are dealing with other patients because their diets are restricted by medical or surgical considerations and because their stay will ordinarily be relatively short. But in the mental hospital the dietitian must not only plan an adequate diet and stimulate the patient's appetite but also promote the patient's interest in eating. Stimulation can be aided by serving out-of-season or specially prepared foods, by variety of cooking style, by the use of food colors in attractive combinations, by the avoidance of foods for which, experience shows, certain patients have developed phobias, or that patients will eschew as a result of religious conviction, or that would embarrass patients in their attempts to consume it, such as steaks for geriatric patients.

Close supervision of sanitation in a mental hospital is especially important. General hospital patients have the capacity to challenge dirty silverware; some mental patients do not. Every effort should be made to see that hot foods are served hot and that cold foods are served cold; mental patients are, if anything, less likely to respond to food at questionable temperatures than anyone else. The same foods should not be served on the same day of every week. Particular desires of the patients should be elicited and, if reasonable, met. At Saint Elizabeths the Patients' Congress, composed of representatives from the various wards, has been invited to make suggestions, with regard to food as well as anything else.

Of course these are counsels of perfection. In actual practice, it often happens that kitchens are too far removed from wards and food is served cold, financial allowances are limited and it is served plain or too often the same, buildings are old and atmosphere is uninviting, equipment is obsolete, attendants will not make the extra effort, patients are uncooperative, and time is short.

But in overcoming all that, too, lies the art.

Science and the Art of Cooking

J. W. Brown, Ph.D.

ELECTROCHEMICALS DEPARTMENT, E. I. DU PONT DE NEMOURS & CO.
WILMINGTON, DEL.

No one can say exactly what elements (other than spiritual) made grandmother's pastries, soups, and main dishes so tasty. As she explained it, a "pinch" of this and a "dash" of that made everything come out just right. But the art of estimating such nebulous quantities and the many excellent recipes undoubtedly veiled therein have yielded to that modern upstart, the scientific method. Today's homemaker can state precisely how she baked that delicious cake: add the entire contents of the package (quantitative transfer) into one and two-thirds cups of water, blend for two minutes at medium speed in the mixer, and bake at 350 degrees for 25 minutes. Considering that the rest of the dinner probably was chipped out of the freezer, there can be little doubt that—in at least one respect—today's cooking has taken on a cold scientific aspect. But the significant feature of this culinary transition is not mere simplicity—it is a shift of the responsibility for choosing and blending basic food ingredients from the homemaker to the food-processing industry. This has resulted in a corresponding shift of much of the responsibility for family nutrition from the home kitchen to the food industry.

By grandmother's standards it might appear that this invasion of the kitchen by science and technology has provided the family cook with an almost disgraceful amount of free time. Yet, it is clear that the fruits of science are not totally sinful and degrading. A consideration of the many varieties of foods from all parts of the world that are now available in all seasons at the local grocery illustrates one advantage. Without modern methods of transportation, refrigeration, and packaging this selection would be impossible. By the use of chemicals in the form of fertilizers, pesticides, and food preservatives, food production has become more efficient, and this advantage has been passed on to the consumer in the form of a greater abundance of foods. These developments have not resulted simply from promotional schemes designed to overstock the local grocery. They met the challenge of a growing industrial economy in which the majority of the people relied more and more on remotely located large scale agriculture for food.

Contributions of equal importance for the present and of greater importance for the future have been made by the science of nutrition. Most notable among past achievements have been the studies of the vitamins and minerals, the accessory factors so necessary to our utilization of the bulk nutrients, protein, fat, and carbohydrate. Early experiments proving that a deficiency of one or more of these trace factors of the diet could result in clinically recognizable disease virtually revolutionized medical thought on the relation of diet to health. Gradually, the importance of these dietary constituents has made its impression on the public, and many homemakers today exhibit a respectable knowledge of vitamins and minerals and the foods that contain them in greatest supply. Such public awareness certainly favors better nutrition for our people and should be encouraged, but there can be little

doubt that by far the most effective and practical measure so far initiated to ensure adequate amounts of these factors in our diet has been the nationwide program of vitamin and mineral enrichment of certain processed foods by the food processors themselves.

More recent advances in nutritional research have provided increasingly abundant data of great practical significance regarding our needs for the bulk nutrients, particularly protein. It may seem strange that our knowledge of these major dietary constituents is not far ahead of our understanding of the quantitatively minor elements, the vitamins and minerals. Yet, it must be remembered that the early recognition of clinical symptoms attributable to a lack of these trace factors undoubtedly dictated a compelling urgency to their investigation. Recently, however, modern techniques of biochemical research have provided data that give nutritionists an entirely new perspective on the complex problems encountered in relating our health to our needs for "just plain food." From these data, and from recent technologic advances, has emerged the practical possibility of improving the protein value of common foods, particularly those based on wheat, through supplementation with synthetic amino acids.

The importance of protein in the diet is obvious, for the amino acids derived from this foodstuff not only form the basic construction of the body, but—when constituted as enzymes—form the "prime movers" that make that construction and the life processes possible. But different dietary proteins can be utilized for these purposes with varying efficiency. High quality protein such as that in meat, milk, or eggs presents the body with a rich assortment of essential amino acids in the amounts and proportions most readily usable, while low quality proteins are much less efficient for the maintenance of health and life. Thus, when considering protein nutrition, one must take into account not only the *quantity* of protein consumed, but also its usefulness as a food—that is, its *quality*.

Nutritionists generally determine protein quality by relating the nitrogen retention or weight gain of experimental animals to the amount of a given protein consumed. If a relatively large amount of the protein nitrogen that is ingested is retained, the protein is said to have high "biologic value." If relatively large weight gains in young growing animals are obtained per weight of protein consumed, the protein is said to be of high "efficiency." Both methods of measurement rate food proteins in a similar order of value. By such experiments it has been found that the protein of whole egg is of the highest nutritional quality. The quality of meat and milk proteins is generally about 60 to 80 per cent of that of whole egg protein, and much lower yet is the quality of many of the proteins of our grain foods. The nutritional value of wheat gluten, the chief protein of wheat flour and the main cereal protein of American diets, is only about 30 per cent of that of egg protein.

However, such great differences in nutritional quality can be largely rectified, particularly with regard to the grain foods, for it is an experimental fact that the quality of the protein of such foods can be improved simply by adding to the grain protein one or more of the amino acids that are essential for the growth of the animal. Since the quality of protein is determined largely, if not entirely, by the amounts and proportions of these essential amino acids, a deficiency in one or more of these

elemental units will result in diminished utilization and decreased nutritional efficiency of the total protein. By comparing the essential amino acid proportions of a given protein to those of whole egg protein, one can predict which amino acid(s) might be primarily responsible for its comparatively lower quality.

Such a comparison in the case of gluten protein of wheat flour would show that one amino acid is in short supply. That amino acid is lysine. By its addition to the wheat flour, the efficiency of the flour protein can be almost doubled. This has been known for many years. But what has not been known is how to obtain sufficient lysine to make this finding of some practical value to our nation's nutrition. Several years ago, a relatively inexpensive method was developed at these laboratories to synthesize this amino acid in bulk quantity, and it is now manufactured as its biologically active salt, L-lysine monohydrochloride. Tests in our laboratories and by others have confirmed earlier experimentation and have demonstrated that the addition of as little as one fourth of a pound of this amino acid salt to every 100 pounds of flour will almost double the nutritional value of white bread baked from this flour.[1, 2] Bread enriched with lysine is being marketed in several areas, and lysine has also been incorporated in several nutritional supplements.

To appreciate the contribution that such research can make to the nutritional well-being of the public, several facts must be considered. Not the least of these, but one of the most neglected, is the fact that bread contains a rather respectable proportion of protein. White bread contains about 8 per cent protein (fresh weight basis) and is equivalent in this respect, pound for pound, to condensed milk.[3] The recently introduced protein breads contain a good deal more, usually 12 to 14 per cent protein, not far below the 16 per cent found in fresh beef hamburger.[3] Without proper supplementation, however, the low biologic value of wheat protein reduces the effectiveness of most breads as protein foods. It is obvious that the addition of sufficient lysine to remedy the natural amino acid imbalance of wheat protein offers an extremely valuable means to raise the protein quality of bread and cereal foods into the range of the animal proteins.

Still another factor to be considered is that there are significant segments of our population—children, old people, families in economically straitened circumstances—that depend heavily on grain foods as a source of protein. While cereal proteins make up only 20 per cent of the total protein consumed by the average American, surveys show that in certain areas of the United States people may depend on grain foods for as much as 40 per cent of their total protein.[4, 5] In fact, the data of Jeans and others would indicate that an increased dependence on cereals for protein is typical in American diets in which consumption of meat, milk, and eggs is below recommended amounts.[6] Individual meals based predominantly on cereal foods occur with increasing frequency in these diets. There can be little doubt that individuals consuming such diets would benefit from a program of amino acid supplementation of bread and other cereal foods.

We must also consider the other extreme—the nutritional problems created by the abundance of our mechanized age. Virtually all jobs, whether they be heavy labor or light housework, have been eased by machinery or new appliances. In many factories, automation has meant that few, if any, employees must perform strenuous

manual labor. In brief, the energy requirements for large numbers of our population have decreased. From a nutritional standpoint, it was inevitable that obesity should arise as a major problem, since a decreased need for energy frequently does not diminish the appetite for calories. Obviously, the "magic prescription" for treatment of most cases of obesity is a reduction in total food consumption so that caloric intake more closely approximates energy utilization. However, the recommended dietary allowances proposed by the National Research Council indicate that the needs of the human adult for protein do not diminish with a decrease in caloric requirements.[7] Thus, if a smaller amount of food is consumed, the diet should be proportionately richer in high quality protein. Otherwise, the countermeasures taken to combat "overnutrition" may result in undernutrition with respect to protein.

In summary, it would appear that amino acid supplementation is one of those rare instances in which two diverse elements of our population can be benefited by the same measures. Supplementation of bread and other cereal grain foods with amino acids provides a prime opportunity to meet the challenge of poor nutrition in some areas and to accommodate the needs resulting from the changing dietary patterns of many others in our general population.

Here, then, is another advantage to the homemaker that has resulted from an invasion of the art of cooking by science and technology. Improvement in the nutritional value of our staple foods could be accomplished only in a situation where the family cook is willing to relinquish some of her culinary domain to a certain amount of industrial processing. Food additives, whether they be preservatives, vitamins, or amino acids, cannot be added in "pinches" and "dashes," but they must be used in the right foods and in the right amounts. Only the food processor, enlightened in these matters and having large mechanical and technical facilities, can act in the public interest and give us these advantages with the degree of assurance required. Past experience clearly indicates that the food industry is alive to this responsibility and more than equal to the task.

BIBLIOGRAPHY

1. Rosenberg, H. R., and Rohdenburg, E. L.: Arch. Biochem. 37:461, 1952.
2. Hutchinson, J. B.; Moran, T., and Pace, J.: Nature *178*:46, 1956.
3. Composition of Foods. U. S. Department of Agriculture Handbook no. 8.
4. U. S. Department of Agriculture Handbook no. 62, 1954.
5. Southern Cooperative Series Bulletin no. 20, 1951.
6. Jeans, P. C.; Smith, M. S., and Stearns, G.: J. Am. Dietet. A. *28*:27, 1952.
7. National Research Council Publ. no. 302, 1953.

Some Nutritional and Therapeutic Aspects of Wine and Cognac

Harold H. Lefft, M.D.

NEW YORK, N. Y.

In countries abroad, even the simplest meal is likely to be accompanied by wine and followed by the leisurely savoring of a cognac brandy. Physicians regard this as a rational aspect of civilized living. Further, they commend the moderate use of wine and cognac as generally beneficial and prescribe both as medication in a number of disorders.[1] Since alcohol is recognized as one of the most ancient of medicines,[2] there is a firm and continuous tradition behind these medical attitudes and a literature rich in references to record it over hundreds of years.

In the United States, however, probably largely because of the Volstead Act of 1919, an entire generation of physicians grew up, were educated, and went into practice virtually without knowledge of the favorable aspects of beverage alcohol.[3] Since then, physicians here (and laymen alike) have been so concerned with the problems of alcoholism that the gains to be derived from the moderate use of wine or cognac have been somewhat obscured.[4]

Thus, while wine and spirits are unquestioned nutritional and therapeutic agents abroad, here in the United States the choice of whether to drink or not is often an emotionally charged decision because of conflicting pressures exerted by various groups. In view of the trend toward increased use of beverage alcohol and the elements of controversy surrounding it, it is more important than ever that the physician be armed with objective, up-to-date appraisals of the subject. A careful scrutiny of the literature reveals much material of interest and significance.

According to recent surveys (Gallup, Riley and Marden, Maxwell) about 65 per cent of the population 18 years and older regularly drink. Jellinek modifies this by stating that some 47,974,660 adult men and women comprise the nonalcoholic consumers of beverage alcohol.[5]

Physicians themselves, according to a recent national study, are moderate users of alcohol. Of those questioned, 80 per cent indicated that they take a drink or so even on weekdays and a few more on week ends.[6] Commenting on this, Davis remarks that physicians now generally "regard moderate drinking certainly as not harmful and often beneficial to their well being."[4]

In relation to treatment, alcohol is probably the most widely taken drug—among laymen at least[7]—being used in a bewildering number of ailments and with considerable conviction. The physician's attitude toward prescribing it now seems to be leaning in the direction recently expressed by Forkner, "Alcohol is a valuable therapeutic agent, just as codeine, demerol or morphine are. Its chief value is that it aids in the dilatation of blood vessels. Hence, at times . . . alcoholic beverages are prescribed with benefit."[8]

EFFECTS OF ALCOHOL

It is well known that ethyl alcohol is an irregularly descending depressant of the central nervous system. Ethyl alcohol is useful as an analgesic and hypnotic; it causes euphoria and "changes the patient's reaction to pain from one of concern to one of relative detachment." Local feelings of warmth, due to action on mucous membranes and on the gastrointestinal tract, the vasodilatation of cutaneous vessels, and "the unrestrained activities of the lower brain centers freed by the depression of higher inhibitory control mechanisms" are the effects seen as "stimulating" by the layman.[2, 9, 10] Yet, these same end results can be most advantageous when deliberately invoked in the patient by a physician aware of both the mechanisms invoked by beverage alcohol and the medical problem at hand.

The notion that alcohol plays a major role in the etiology of hepatic cirrhosis has never been demonstrated conclusively.[2] It has been thoroughly reported that this disease is one of deficiency and is seen both in the livers of alcoholics and in subjects who do not drink at all. In fact, Joliffe has commented that excessive ingestion of sweet carbonated beverages is as likely to produce cirrhosis as is chronic alcoholism.[11]

Another questionable notion concerns the deleterious effects of alcohol on renal function. In fact, ethyl alcohol is an excellent diuretic and in moderate quantities is not contraindicated. As in cirrhosis, it has not been fully demonstrated that the kidney abnormalities of heavy drinkers can be attributed to the alcohol they ingest. Goodman and Gilman state, "with the possible exception of some individuals with arteriosclerotic nephritis, the ingestion of varying amounts of alcohol or whiskey has no deleterious action on renal function in normal subjects or in patients with acute or chronic nephritis."[2]

Alcohol is a readily available source of energy for muscular work. While it has been concluded that alcohol disappears from the human body at a uniform rate whether the subject is at rest or is exercising, its vasodilatative effect probably increases muscular circulation and induces a lessened awareness of being tired, making a greater volume of work possible.[9]

The subjective effects of alcohol are one of its aspects that make it unusually useful in the hands of the physician. Thus, a physician may be well aware of the objective evaluation of the effect of alcohol on the heart, circulation, and brain; he may prescribe a drink of cognac for a patient suffering from hypertension, for example, not only to achieve these effects directly but because he recognizes that on drinking the cognac the patient will begin to "feel better" almost at once. As the cognac proceeds to relax his tensions, the patient becomes less affected by his conscious and unconscious fears and anxieties. And as he "feels better" this subjective effect will, in turn, influence his physiology.

IN NUTRITION

Alcohol is quickly absorbed from the gastrointestinal tract, requiring no preliminary digestion, and thus is utilizable as energy more rapidly than other foods. Unlike other foods, it is metabolized at a constant rate regardless of the quantity

present. The energy released per gram of ethyl alcohol is approximately 7 calories and, to this extent, can substitute for other energy sources. It also conserves other energy materials (protein, for one) and does not increase basal heat production. Alcohol does not impede stomachic or intestinal digestion when consumed in moderate quantities; in fact, it is seen as a mild digestive stimulant, increasing the ability of the gastric glands to secrete free hydrochloric acid. It does not impair gastric motility when ingested moderately, and the secretion of pancreatic juice "may actually be stimulated by small doses of alcohol."[2, 9] Only when alcohol is consumed excessively is it considered a contributor to pancreatitis.[12]

A number of investigators have noted that in wine, or in spirits distilled from wine such as cognac, trace elements of minerals and vitamins from the original soil in which the grapes grow, as well as elements such as purines, pectins, fats, levulose, and dextrose, can contribute valuable dietary adjuncts.[3] In addition, the calorie content (in spirits it can be roughly estimated per drink as equivalent to the proof—cognac, for example, yields about 80 to 84 calories/ounce) can be useful as an addition to diets for the underweight, or in diabetes, since many feel that insulin is not required to metabolize alcohol.[13, 30] And, on the subject of geriatric patients, Levy has remarked, "we all probably agree that a little alcohol is a good thing rather than the reverse."[14] The liquid form and the pleasing flavor in a beverage such as cognac make it especially useful in treating the aging.[26]

Since the days of the Greeks and Romans, wines and spirits have occupied prime positions in the armamentarium of the chef. As a flavoring agent, by marination or as an integral part of a recipe; as a preservative; in breaking down and blending with other foods by "rinsing" a pan, in the preparation of sauces; in contributing to visual appeal by "blazing"—these are among the contributions made to cookery and to the enjoyment of eating by wine and/or cognac brandy.

Hunger and appetite together constitute the complex sensation that causes human beings to seek food and to consume it. Hunger and appetite, however, are seen to differ fundamentally from each other. Appetite sometimes appears to influence people more greatly than hunger. An example is the phenomenon seen sometimes in patients after gastrectomy or vagotomy, in whom "hunger pangs" persist relentlessly although they must inevitably have been removed by the surgery. Thus, as noted by Goetzl, "these and other observations lead one to believe that extragastric stimuli are importantly involved in producing the hunger experience . . . the sensation of appetite suffices to insure ingestion of a proper supply of nutriment."[15]

Beverage alcohol in moderate quantities is an unparalleled stimulator of appetite. It impels increased flow of saliva and gastric juice and reduces consciousness of psychic factors that can contribute to anorexia. In addition, by stimulating the gastric mucosa, alcohol causes a sensation of warmth within the stomach, raises the gastric tone, and by these means adds to appetite.[9] Pavlov has reported his own experience in restoring lost appetite following an illness by the drinking of a wine.

Used as an apéritif before meals, a whiskey or cocktail, a fortified wine such as sherry, or an aromatic spirit such as cognac, rich in flavor from its congeneric substances, may be the ideal prescription for a flagging appetite. In the malnourished, the convalescent, or the aged,[30] such a drink before the main meal of the day may be

all the encouragement necessary for the attainment of a more desirable dietary status. Between meals it may be beneficial for such patients to drink a mixture of eggs beaten into milk to which has been added cognac or some other pleasingly flavored beverage alcohol.

Further, it has been suggested that the feeling of satiety that reduces appetite prematurely, cuts down on the quantity of food consumed, or prolongs the interval between meals to undesirable lengths may be prevented by the consumption of moderate amounts of a beverage alcohol (particularly wine) before a meal, during it, or immediately after.[16, 37]

IN CARDIAC AND CIRCULATORY PROBLEMS

Cognac has long been recognized as a treatment of choice in syncope. "The time-honored use of brandy in a syncopal attack is therefore justifiable," states Sears, "although smelling salts or sal volatile are equally effective, but in these days less readily available even than brandy."[17] White also mentions brandy favorably in the treatment of vascular shock.[18] The well known effectiveness of brandy in fainting is due to the reflex stimulation of the mouth, throat, and stomach.[2, 18]

Beverage alcohol increases peripheral vascular flow and thus is of value in the treatment of patients who suffer from insufficient circulation—especially the aged.[38] When such patients avail themselves of it "in suitable moderation . . . the feeling of chilliness is lessened by the flow of blood to the skin, and the mild sedative action of the alcohol relieves some of the aches and pains."[19] Steiglitz also recommends the use of alcohol; "it is of considerable assistance in the management and control of arteriosclerotic change in elderly persons."[20]

Samuels prescribes alcohol in thromboangiitis obliterans and in arteriosclerosis obliterans: "It may be given in the form of whiskey or wine of high alcoholic content . . . Alcohol is an effective vasodilator and may be prescribed freely . . . unless there is some constitutional contraindication."[21]

Wright states, "Alcohol has definite vasodilating effects on the peripheral arteries. Experiments carried out in our labs showed, following the ingestion of 60 to 90cc (2 to 3 oz.) of whiskey a rise in temperature of the tips of the extremities as great as 6-7 degrees . . . depending on the condition of the vessels and the control level preceding the experiment. We feel therefore that the use of whiskey or other spirituous liquors is indicated in the treatment of organic occlusive peripheral vascular diseases, among the most important of which is arteriosclerosis. There is a widespread agreement regarding this.

"The dosage depends on the severity of the condition and the tolerance of the individual. With impending gangrene the patient should receive enough alcohol in any palatable form of the patient's choice to keep the peripheral vessels as dilated as possible. . . . Brown and Allen pointed out that in addition to vasodilating properties, whiskey may control the pain in some cases of peripheral vascular disease more satisfactorily than morphine."[22] In discussing thromboangiitis obliterans, Wright adds, ". . . after the acute stage has passed the patient should have two cocktails or highballs each evening to encourage vasodilation of the remaining

functioning vessels."[22] In acute arterial occlusion, Wright states, "Alcohol is freely given in the form of whiskey or brandy with 1 to 2 oz. every three or four hours, depending on tolerance."[22]

In discussing various aspects of 100 patients who survived heart attacks, Luongo notes that "71 per cent have been using alcohol in moderation anywhere from 1 to 10 years since the attack. In this group all claim beneficial effects, with less anxiety. While one cannot relate any beneficial effects of alcohol directly to improved coronary blood flow, there is evidence in the literature that in moderation alcohol may diminish the work load of the heart by reducing the pressure in the small peripheral arteries of the body. More important, alcohol in moderation may relieve anxiety through cerebral action. This anxiety frequently contributes to the onset of heart pain."[23]

After many years of discussion of coronary artery flow, the consensus now appears to be that plain ethyl alcohol has little or no influence.[2] Recently, however, evidence has become available that the congeneric factors of certain beverage alcohols appear to have a definite effect on the coronary arteries in animal hearts. This may lead to re-evaluation in the case of man. Vartianen et al "undertook to study the effect of various aromatic and slightly aromatic alcoholic drinks on the coronary flow of the isolated rabbit heart."[24] They came to the conclusion that in the case of a cognac brandy with rich flavor (a 20 to 25 year old cognac was used in the tests along with plain ethyl alcohol, cheap brandy, and arrack) coronary artery flow definitely increased. "A total of 40 tests were carried out. Pure ethyl alcohol was found to have a very slight vasodilating effect on the coronaries. Old brandy with rich aroma was found to be a clearly more effective coronary vasodilator than ethyl alcohol or crude colourless distillate of wine with few aromatic substances. . . . The use of old aromatic brandy may be advisable . . . by the side of other drugs but the matter has to be given careful consideration in each individual case."[24]

Since William Heberden's classic description of angina pectoris in 1772 accompanied by the advocation of "spirituous liquors,"[25] physicians have been prescribing beverage alcohol for patients with this disease.[33, 34] Whether it is because it is believed that coronary artery flow is aided, or because of the analgesic and anxiety-relieving properties of alcohol, physicians continue to do so today. Noting that beverage alcohol has enjoyed a long and respectable history as a therapeutic aid in angina pectoris, White says, "the most effective drug after nitrates is alcohol. . . . An ounce or two of whiskey, brandy or rum may give rapid relief . . . usually in the course of a very few minutes."[18] It is also useful in the prevention of attacks.[18] Russek, Naegele, and Regan concur: "Alcohol . . . is rated by most contemporary authorities as one of the few effective coronary vasodilators, second only to the nitrites. Indeed, the effect of 1 or 2 ounces (30 to 60cc.) of whiskey or brandy in terminating an anginal attack is said to be comparable in many instances to the results obtained with glyceryl trinitrate. Nevertheless, it is in the prevention rather than in the treatment of these episodes that alcohol has been deemed of particular clinical value. Physicians frequently prescribe it in angina pectoris as a routine prophylactic measure and especially before contemplated effort or excitement. . . . Its beneficial influence in angina pectoris may . . . arise from its sedative action,

through which it increases the threshold for pain sensation without exerting any significant effect on underlying myocardial anoxia."[26]

Stewart, discussing the advisability of prescribing a drug that relieves pain but does not seem to affect the underlying condition, states, "Brandy or whiskey may be used to give relief from an attack, or as a preventive measure. . . . For my part, I allow patients moderate amounts of alcohol daily as medication. . . . The beneficial effect of alcohol may be in part attributed to its analgesic effect."[27]

Friedberg comments, "While I always permit and usually advise the ingestion of moderate amounts of alcohol by patients with angina pectoris, especially elderly patients, I do so more for its beneficial effect on general well-being than for any dramatic improvement in the angina pectoris itself."[28]

Levine says, "Alcohol in the form of suitable drinks is often of considerable help either during a spell or, better still, as a preventive. Some individuals find ½ to 1 ounce . . . taken before bedtime will prevent attacks from coming at night."[29]

And, mentioning the analgesic effect of alcohol, Cecil and Loeb add, "Alcohol in small amounts is usually well tolerated; especially in the elderly. Brandy or whisky, 15 to 30cc. for the prevention or relief of attacks may be useful."[10]

In our treatment of various cardiovascular and circulatory ailments at this health center, we have had an opportunity to study the effects of cognac brandy on these ailments. In moderate quantities these spirits primarily stimulated and then relaxed the patient. Moreover, these spirits are "salt-free" and have a tendency physiologically to promote diuresis. In cases where appetite is poor, they improve the eating habits of the patient.

Many of the cardiovascular or circulatory diseases, and other disease conditions as well, are associated with a marked degree of insomnia, probably due to concomitant cerebral pathology. The ordinary hypnotics have an antagonistic effect on these patients, and after one or two hours of sleep they become wide awake and find it impossible to return to sleep. Moreover, patients develop a resistance to these drugs and eventually require larger doses. As a result they awake each morning with a stuporous feeling and drowsiness. Often they become addicted to these hypnotics and develop an abnormal sleep mechanism. This situation will eventually aggravate the pre-existing condition, and a vicious cycle thus becomes effectuated.

With the use of cognac brandy as a form of vasodilating or relaxing mechanism, the individual does not feel that life has become a hazard, nor does he feel that he has suddenly become ostracized because of an ailment over which he has no control.

In the opinion of White[15] and others, brandy and other types of beverage alcohol are useful in insomnia. The mildly sedative effect and the relief from anxiety that alcohol affords result in pleasant sleep.[30]

OTHER USES

For the common cold, laymen and physicians alike rely on alcohol. One old prescription involves hanging a hat on the bedpost and drinking away until two hats appear to be present.[2] A bit more moderation is used in today's prescriptions of alcohol, varying "from 39 to 90 cc. (1 to 3 oz.) depending on the patient's toler-

ance."[21] Bastedo recommends taking the brandy immediately after exposure to prevent a cold or, if a cold is already in residence, to check it.[22]

For emesis gravidarum, iced champagne or iced brandy is seen as helpful.[22] For seasickness they are also useful.

The analgesic effects of alcohol are also useful in the treatment of arthritic patients, according to Cecil and Loeb and to Davis. "A small drink of whiskey will do much to brighten the end of the day for the arthritic patient and usually gives definite relief from pain," remark Cecil and Loeb.[10] Davis adds, "Even in gout, it appears that moderate drinking is non-harmful; and, in fact, my own work has led me to a number of cases in which beverage alcohol has had marked analgesic effect."[4]

SUMMARY

The moderate ingestion of beverage alcohol, especially wine and cognac, is seen as generally productive of a sense of well-being. Wine and cognac are widely accepted as aids in nutrition, to stimulate appetite, and in therapy of various cardiac and circulatory diseases. Alcohol in these and other forms is also of value in relieving feelings of anxiety, worry, and fear, in providing analgesia in certain painful conditions, and as a sedative and soporific. Wine and cognac are especially useful in the treatment of geriatric patients.

BIBLIOGRAPHY

1. Jackson, G. H.: The Medicinal Value of French Brandy, Montreal, Therien Freres Ltd., 1928.
2. Goodman, L. S., and Gilman, A.: The Pharmacological Basis of Therapeutics, ed. 2, New York, The Macmillan Co., 1956.
3. Lucia, S. P.: Wine as Food and Medicine, New York, The Blakiston Co., 1954.
4. Davis, J. S.: The medicinal benefits of beverage alcohol, Virginia M. Monthly *84*:3–7, Jan., 1957.
5. Jellinek, E. M.: Distribution of alcohol consumption and of calories derived from alcohol in various selected populations. *In:* Alcohol and Its Nutritional Significance, Proceedings of the Nutrition Society, March 12, 1955.
6. The care and feeding of the doctor (the inner man), Med. Economics 32:117, Dec., 1955.
7. Liebman, S., ed.: Management of Emotional Problems in Medical Practice, Philadelphia, J. B. Lippincott, 1956.
8. Forkner, C. E.: Personal communication.
9. Best, C. H., and Taylor, N. B.: The Physiological Basis of Medical Practice, ed. 4, Baltimore, Williams & Wilkins Co., 1945.
10. Cecil, R. L., and Loeb, R. F.: Textbook of Medicine, ed. 9, Philadelphia, W. B. Saunders Co., 1955.
11. Joliffe, N.: Alcohol and nutrition; the diseases of chronic alcoholism. *In:* Alcohol Science and Society, ed. 6, New Haven, Quarterly Journal of Studies on Alcohol, 1954.
12. Sterling, J. A.: The Biliary Tract, Baltimore, Williams & Wilkins Co., 1955.
13. Fishbein, M.: Fads and Quackery in Healing, New York, Covidi-Friede, 1932.
14. Levy, R. L.: Panel discussion on heart disease, J. Am. Geriat. Soc. *4*:843, Sept., 1956.
15. Goetzl, F. R.: Human appetite, Permanente Found. M. Bull. *8*:2, April, 1950.
16. Dona, I. L.; Dura, A., and Goetzl, F. R.: Influence of tannic, tartaric and of acetic acid upon olfactory acuity and sensations associated with food intake (a note concerning the appetite stimulating effect of wine), Am. J. Digest. Dis. *20*:17–21, Jan., 1953.
17. Sears, W. G.: The medical indications for alcohol, Practitioner *168*:427–429, 1952.
18. White, P.: Heart Disease, New York, The Macmillan Co., 1951.
19. Haggard, H. W., and Jellinek, E. M.: Alcohol Explored, New York, Doubleday Doran & Co., 1942.

20. Steiglitz, E. J.: Nutrition problems of geriatric medicine, J. A. M. A. *142*:1070–1077, 1950.
21. Samuels, S.: Management of Peripheral Arterial Diseases, New York, Oxford University Press, 1950.
22. Wright, I.: Vascular Diseases in Clinical Practice, Chicago, Yearbook Publishers, Inc., 1952.
23. Luongo, E. P.: Health habits and heart disease—challenge in preventive medicine, J. A. M. A. *162*:1021–1024, Nov. 10, 1956.
24. Vartianen, O.; Venho, E. V., and Vapaavuori, M.: Influence of various alcoholic beverages on coronary flow, Ann. med. int. Fenniae *42*:162–173, 1952.
25. Heberden, W.: Some account of a disorder of the breast, M. Tr. Roy. Coll. Physicians *2*:59–67, 1786.
26. Russek, H. I.; Naegele, C. F., and Regan, F. D.: Alcohol in the treatment of angina pectoris, J. A. M. A. *143*:355–357, May 27, 1950.
27. Stewart, H. J.: Cardiac Therapy, New York, Paul B. Hoeber, Inc., 1952.
28. Friedberg, C. K.: Diseases of the Heart, ed. 2, Philadelphia, W. B. Saunders Co., 1956.
29. Levine, S. A.: Clinical Heart Disease, Philadelphia, W. B. Saunders Co., 1952.
30. Rolleston, H.: Alcohol in medicine, Practitioner *113*:209–214, 1934.
31. Barr, D., ed.: Modern Medical Therapy in General Practice, Baltimore, Williams & Wilkins Co., 1940.
32. Bastedo, W. A.: Pharmacology, Therapeutics and Prescription Writing, Philadelphia, W. B. Saunders Co., 1948.
33. Russek, H. I.: Drug therapy in angina pectoris, J. Am. Geriat. Soc. *4*:877–879, Sept., 1956.
34. Master, A. M.: Angina pectoris—a thirty-year progress report, J. A. M. A. *162*:1542–1544, Dec. 22, 1956.
35. Berry, C. W.: A Miscellany of Wine—Wine and Its Medicinal Uses, London, Constable & Co., 1932.
36. Stearns, S.; Riseman, J. E. F., and Gray, W.: Alcohol in the treatment of angina pectoris, New England J. Med. *234*:578–582, May 2, 1946.
37. Irvin, D. L., and Goetzl, F. R.: The influence of tannic acid upon olfactory acuity and the sensation complex of appetite and satiety, Permanente Found. M. Bull. *9*:119–124, Oct., 1951.
38. Marvin, H. M.; Wright, I. S.; Page, L. H.; Jones, T. D., and Rutstein, D. D.: You and Your Heart, New York, Signet, 1953.
39. Greco, G. F.: Hypertensive heart disease, Geriatrics *5*:15–25, 1950.

SYMPOSIUM ON MEDICINE AND WRITING

The Symposium on Medicine and Writing that appeared in the November 1956 issue of International Record of Medicine has been published recently as a Monograph. The articles included in this Monograph are: "The Editing of a Modern Medical Textbook" by Russell L. Cecil; "Plain Talk and Clear Writing" by Morris Fishbein; "The Principles of Bibliographic Citation" by John F. Fulton; "The Art of Communication" by Joseph Garland; "On Writing a History of Medicine" by Douglas Guthrie; and "Minerva and Aesculapius: The Physician as Writer" by Félix Martí-Ibáñez.

This 72 page Monograph is sold for $3.00. As the fourth in the series of MD International Symposia, this book is the companion piece of *Medical Writing*, which was published in May 1956.

To obtain this monograph, write to MD Publications, Inc., 30 East 60th Street, New York 22, N. Y.

NATIONAL HEALTH SURVEY BEGUN. The National Health Survey has been launched by the Government to compile nationwide statistics on accidents, disabilities, hospitalization, illnesses, and medical care. Three thousand households are being checked each month, with separate data being collected in eight metropolitan areas. The survey is expected to be the first reliable one of its type in almost 25 years.

WALKING FOUND SUCCESSFUL TREATMENT FOR GANGRENE. Amputations were avoided and gangrenous condition healed in 21 of 22 patients encouraged to walk around despite gangrene of the feet and legs, reports William T. Foley (Circulation, May). The usual procedure in cases of gangrene is to confine the patient to bed. The one failure in this series was a patient whose family refused to let her walk after she left the hospital; she required amputation a few months later.

PROMISING RESULTS IN LEUKEMIA CASES. 6-Azauracil, one of the azapyrimidines, produced "important therapeutic effects in...acute leukemia cases, primarily among children," report B. I. Shnider and associates (National Cancer Institute). The drug was administered orally for periods up to 90 days to 44 adults and children with leukemia.

NEW TECHNIQUE IN INTRACARDIAL PHONOCARDIOGRAPHY. A new technique in intracardial phonocardiography, with sound vibrations being registered from the end of an ordinary catheter and through an amplifier connected to the electrocardiograph, was reported by Aldo A. Luisada at the Institute of Cardiology (Mexico City). Sounds and murmurs can be studied in the left as well as the right side of the heart, an extremely fine catheter being introduced for the left side.

ULCER PATIENTS CAN EAT MANY SPICES. Ulcer patients can safely eat cinnamon, allspice, thyme, mace, sage, paprika, and caraway seed without feeling discomfort or interfering with healing time of the ulcer crater, but they should not eat black pepper, mustard, chili pepper, cloves, and nutmeg. A test with 50 patients showed these findings, report physicians at Peter Bent Brigham Hospital (Boston). They hope

the use of prescribed spices will speed the recovery of ulcer patients by overcoming their reluctance to adhere to the usual bland diet.

INCIDENCE OF CONGENITAL ANOMALIES. About 8 of every thousand infants have a congenital anomaly, according to a five year study of all births in Pennsylvania. Five most common anomalies: clubfoot, cleft lip and/or palate, superfluous fingers, spina bifida, hypospadias.

CYANIDE POISONING TRACED TO FROZEN CELERY. An investigation on the West Coast has disclosed that a number of cows recently died from cyanide poisoning after eating celery tops damaged by frost. Chemical analysis showed that free cyanide develops in celery that has been frozen, and the matter is being investigated further to determine the significance of these findings from the consumer standpoint.

NO WITHDRAWAL SYMPTOMS WITH MEPROBAMATE IN 300 PATIENTS. No instance of withdrawal symptoms, a sign of habituation, was reported in the treatment of more than 300 psychiatric patients with meprobamate (Miltown, Wallace Laboratories) in a 2½ year period at Albany Hospital (J.A.M.A. 163:489, 1957). Albany Hospital patients are never tapered off the drug, and although some patients had been on the drug for as long as 15 months, no withdrawal reactions were seen when it was suddenly discontinued.

LYSINE IMPROVES PROTEIN VALUE OF BREAD. Addition of lysine to bread already enriched with milk solids greatly improves its protein value, report Purdue University nutritionists. In laboratory experiments, rats fed 3 parts of milk solids to 100 parts of flour, plus small amounts of lysine, showed growth comparable to rats fed 12 parts of milk solids without lysine. Also, rats fed a bread misture containing 12 parts of milk solids plus lysine, salt, cod liver oil, and vitamins grew at an average rate only slightly less than that of rats fed an optimal diet high in protein and all other required nutrients.

CHEMICAL PROTECTS AGAINST RADIATION. A chemical known as AET (beta-amino-ethyl-iso-thiuronium-Br-HBr) has been found to protect monkeys against lethal doses of whole body radiation, report B. G. Crouch and R. R. Overman in Science. Dosage used is 150 to 250 mg./Kg. body weight, administered before irradiation. Previously, AET was found to give 100 per cent survival in mice that received a dose of whole body radiation 100 per cent lethal to untreated mice.

Chlorpromazine as an Adjunct in Managing Tuberculous Patients

Harry Shubin, M.D., Charles A. Heiken, M.D., Allen Glaskin, M.D., Edward Pennes, M.D., and J. Arsenian, M.D.

PHILADELPHIA GENERAL HOSPITAL, NORTHERN DIVISION, AND RUSH HOSPITAL
PHILADELPHIA, PA.

The management of patients with pulmonary tuberculosis has always involved a seeming contradiction. The nature of the disease demands a relatively long period of treatment and recuperation; at the same time, the enforced inactivity during this period tends to cause emotional stresses that disrupt treatment and consequently interfere with healing processes. Happily, presentday chemotherapy has shortened the period of hospital care for many, but in one sense this advance in treatment is a double-edged sword. Because of the progress we have made, public apathy toward tuberculosis has developed, and often the patient, feeling that a simple cure is available, refuses hospitalization, preferring to be treated at home as an ambulatory patient. This despite the fact that, even with the advent of drugs that inhibit the tubercle bacillus, most of those afflicted, if not all, still require an initial period of hospital care, while many of those with persistently active tuberculosis should have prolonged hospitalization.

Admittedly, the prospect of spending one or two or more years in a hospital is not a pleasant thought. Added to the strains on personality occasioned by the knowledge that one has a disease publicized in the past as a "vicious killer" are the anxieties of family separation, loss of contact with one's job, and the need of adjusting to a new environment. And all of these strains are intensified by the enforced quiet and rest of a tuberculosis regimen. Tollen[1] cogently points out: "While the body rests, emotional and psychic energy accumulate. These cannot be freely discharged in activity, because for the tuberculous patient the motto must be: 'All possible avoidance of activity.' The energy, therefore, manifests itself in tensions and irritability. The behavior of the patient becomes 'unreasonable.' It takes a balanced, well-supported personality to overcome the contradiction inherent in treatment for tuberculosis."

Contributing to the problem is the overcrowding of tuberculosis hospitals, which has forced the treatment of many on an outpatient basis. This in turn demoralizes those who are hospitalized; they want to return home, get back on the job, and pursue treatment outside the hospital. At home, they fail to take, or take irregularly, the prescribed drugs, are unfaithful to the requirements of rest, etc. More culpable is the lack of vision of which many of us have been guilty in not taking steps to make the time of "confinement" more bearable. We provide the best medical and surgical care but pay scant attention to the patient as an individual. We furnish little rehabilitation or occupational assistance, leaving him to stare at his four walls, his fellow patients, or television (assuming it is in working order). Naturally, such an atmosphere creates unhappiness, unrest, and general dissatisfaction and has con-

tributed to the high rate of "absenteeism" or unsanctioned discharges among tuberculous patients.

We have found in our experience that the problem of managing the tuberculous patient involves three specific types: (a) The recently diagnosed case. During the weeks immediately after the discovery or flare-up of symptoms, the patient is usually most cooperative. But after this initial period, when toxic effects abate and he no longer "feels sick," he tends to become apprehensive about his absence from home and job and accepts hospitalization only reluctantly. (b) The chronic patient, with a history of fibroulcerative disease not amenable to surgery, yet with persistently positive sputa. He requires prolonged observation and chemotherapy, but because he is not acutely ill and often has the sense of being a "veteran" with special privileges, he creates ward difficulties, "goes AWOL" repeatedly, etc. (c) The court-committed patient, who has been forcibly hospitalized because of constantly "going AWOL" or failing to cooperate with health agencies as an outpatient. He is likely to be antagonistic and belligerent from the start, often has a criminal record or tendencies, and proves a real problem in management.

It is the "management problem" in tuberculosis therapy that led to the present study. In February 1956, when it was undertaken, we were, of course, familiar with the extensive literature on chlorpromazine attesting to its usefulness in relieving anxiety, tension, and apprehension and in controlling hard-to-manage patients, nonpsychiatric as well as psychiatric. We were thus interested in evaluating this drug as an aid in the care and rehabilitation of individuals afflicted with pulmonary tuberculosis.

MATERIAL

Eighty-two patients in four tuberculosis wards comprised the study group. All had active pulmonary tuberculosis as shown by roentgenogram and sputum analysis. Thirty-two were men; 50 women. Their ages ranged from 14 to 86, though more than half the group were within the 30 to 50 year age bracket.

In accordance with the described analysis of the problem, patients were divided into three groups: (a) recently diagnosed, (b) chronic, (c) court-committed.

METHOD

We employed a double-blind placebo-controlled study, that is, neither the staff (physicians, nurses, attendants) nor the patients knew which was the active or inactive drug. Placebo tablets and tablets containing the active drug were identical in appearance and were identified only by code until the evaluation was concluded, in dosage of 25 mg. three times daily.

Each type of tablet was administered three times daily to half the patients in each of the four wards. Four of the five man team of observers carried out the routine ward administration and reviewed their findings with the senior member, who acted as a neutral observer. Patients were under observation for from one to six months, the average duration being five months. Records were kept for all patients, with progress reports prepared once monthly.

Results were rated according to the following values: (a) ***negligible*** meant the

patient displayed anxiety and guilt feelings, restlessness; was uncooperative, "went AWOL"; (b) *moderate* meant the patient had become relaxed and quiet, in contrast to pretreatment behavior, and cooperated in ward routine and treatments; (c) *marked* meant the patient had adjusted emotionally to his disease, realizing the merits of continuing treatment in the hospital, although opposed to this initially.

We recognized the "human error" involved in expressing personal opinions regarding mental profile. It was not, however, possible to have psychologic evaluations made; nevertheless, the investigators had been working with the patients for sufficient time to know them emotionally as well as physically and to judge any change in behavior.

RESULTS

Table I summarizes the results observed in this series. Two main points emerge from our findings: (1) Chlorpromazine is a useful adjunct in managing tuberculous patients who, because of emotional distress, approach treatment with an attitude that is not conducive to successful rehabilitation. There is no doubt of its utility when the favorable results are contrasted with those in patients given placebos. (2) Effect on action of specific antituberculous drugs: No noticeable change in the therapeutic effect of antituberculous drugs was seen with the added use of chlorpromazine. Indicated drug or surgical therapy was undertaken in either chlorpromazine-treated or "control" patients with comparable results. Side effects: Slight drowsiness was noted in approximately 15 per cent of the chlorpromazine-treated patients, but subsided usually within the first week or two of treatment. In some patients, this effect was desirable. Jaundice developed in 1 patient but cleared up spontaneously even though drug treatment was continued.

DISCUSSION

Although not many patients were involved in the "recently diagnosed" group, the results here were sufficiently promising to suggest that the tranquilizing property of chlorpromazine helps to cushion the emotional letdown that often occurs after

TABLE I

Results Observed in the Series

Type of patient	No. patients	Marked		Moderate		Negligible	
		P*	CZ†	P*	CZ†	P*	CZ†
Recently diagnosed	12	—	2	—	2	7	1
Chronic	60	—	5	1	26	23	5
Court-committed	10	—	—	—	2	6	2
Total	82	0	7	1	30	36	8

* P = Placebo, three times daily.

† CZ = Chlorpromazine, 25 mg. three times daily.

the first few weeks of care. The patient is less apprehensive, less likely to oppose unreasonably any suggestion about the possible need for surgery or a long period of hospital care.

With the "chronic" cases, the gain in cooperation was substantial, while not often dramatic. The absenteeism record among the chlorpromazine-treated patients was reduced from 30 per cent before the study period to 15 per cent in the course of the study. Furthermore, although it is sometimes difficult to localize behavioral outbreaks in any chronic disease ward, we did feel that there were fewer disturbances caused by patients on chlorpromazine than by those receiving placebos. The facts that negligible side effects were noted and that there was no antagonism to antituberculous therapy point up the merits of reinforcing the usual chemotherapeutic regimen with drugs that alleviate emotional stress.

Only a small number of court-committed patients were studied, but even here the chlorpromazine group were temporarily more cooperative, though little real hope exists for these patients unless some program of psychiatric counseling is provided.

These results would seem to indicate that the drug is a valuable aid in therapy. At the same time, they make it clear that such treatment plays only a supporting role in rehabilitating the patient. The source of his anxiety remains, but by relieving tension, the drug paves the way for the physician to orient his patient in regard to the disease and the steps in treatment.

In the final analysis, we must always stress that with tuberculosis more than with most other diseases it is necessary to deal with the total patient and not only with the physical aspects of his illness. On this point, Tollen,[1] surveying the problem of "irregular discharge" in veterans' tuberculosis hospitals, writes: "Those concerned with the physical manifestations of tuberculosis must never forget that psychic factors are generally present. . . . Anxiety and fear are the most common characteristics manifested in the behavior of tuberculous patients. An uncommon strength of personality is required to withstand the psychic burden of hospitalization. . . ."

What is needed ultimately is a comprehensive rehabilitative program, a program involving a medical-surgical team, psychiatrist, psychologist, occupational therapist, and social workers.

One part of this kind of program might be centered in group therapy, whereby a psychiatrist could meet with a number of patients to discuss and resolve general personality problems concerning adjustment to hospital routine. There might also be informal talks by persons who have recovered from tuberculosis reassuring patients that success can be obtained, that surgery and chemotherapy alone are insufficient, that hospitalization plays a key role in treatment and rehabilitation, that a productive life awaits the patients after recovery.

SUMMARY

For a period of six months, 82 patients with active pulmonary tuberculosis were studied in regard to the use of chlorpromazine as an adjunct to antituberculosis chemotherapy.

Of 45 patients on chlorpromazine therapy, 18 per cent showed "negligible" results,

67 per cent showed "moderate" improvement in cooperation and disposition, and 15 per cent showed "marked" improvement.

Drowsiness occurred in 15 per cent of the patients but subsided in the first week or two of the study. Jaundice developed in 1 case but cleared spontaneously as the therapy continued.

CONCLUSION

Chlorpromazine effectively reduces the stresses of tuberculous patients and makes them more amenable to and cooperative with medical-surgical advice; at the same time, the partial success of this treatment, directed to the nonphysical manifestations of the disease, serves to reinforce the opinion of many in the field that the most effective program against tuberculosis will be based on a comprehensive medical-surgical psychologic program.

ACKNOWLEDGMENT

We wish to thank Smith, Kline & French Laboratories and Joseph Cassen for supplying the chlorpromazine and for assistance in this study. The trade name of Smith, Kline & French Laboratories for chlorpromazine is Thorazine.

BIBLIOGRAPHY

1. Tollen, W. B.: Irregular Discharge: The Problem of Hospitalization of the Tuberculous, Washington, D. C., Veterans Administration Pamphlet 10-27, 1948, pp. 7, 45.

Fifth Annual Symposium on Antibiotics

We are pleased to announce that the Fifth Annual Symposium on Antibiotics, sponsored by the Food and Drug Administration, Division of Antibiotics, U. S. Department of Health, Education, and Welfare, with the journals, Antibiotics & Chemotherapy and Antibiotic Medicine & Clinical Therapy, will be held on October 2, 3, and 4, 1957, at the Willard Hotel in Washington, D. C.

Submitted manuscripts must contain new, previously unpublished material. They must be typewritten, double spaced, on one side of 8½ by 11 inch paper. No more than six illustrations should accompany each manuscript. These glossy prints should be no larger than 8½ by 11 inches so that they can be clearly reproduced with a one third reduction. Bibliographies should conform to the style of the *Quarterly Cumulative Index Medicus*, published by the American Medical Association. Generic names of drugs should be used throughout the manuscript, except that the first time the drug is mentioned the trade name may be referred to in a footnote.

The original manuscript and one copy must be submitted by September 2, 1957. Five copies of an abstract of no more than 200 words must be submitted no later than August 19, 1957. Please submit manuscripts to:

Dr. Henry Welch, Director
Division of Antibiotics
Food and Drug Administration
U. S. Department of Health, Education, and Welfare
Washington 25, D. C.

MEDICAL INSTRUMENTS SECTION*

The Role of Electrophoresis in Medicine

Miriam Reiner, Ph.D.

CHEMISTRY LABORATORY, DISTRICT OF COLUMBIA GENERAL HOSPITAL
WASHINGTON, D. C.

INTRODUCTION

Since 1940, there has been an increasing utilization of physical chemical methods in the field of medicine. There have been wide and varied applications of the principle of electrophoresis from the time that various types of apparatus based on the ideas of Tiselius[1] and Svensson[2] became available for the moving boundary method.

Electrophoresis may be defined as the migration of charged particles in an electrical field toward the oppositely charged electrode. In the moving boundary method, the progress of the boundaries formed between colloidal (such as protein) and buffer solutions may be followed optically. This is possible due to the *schlieren* differences in refractive index between the buffer and the protein fractions at the boundaries. The mobility of the fraction or substance may be calculated under controlled conditions by measuring the distance it has traveled from the starting point. The relative concentrations of a mixture of proteins such as blood serum is determined by observing on a screen the extent of the refraction of light at the boundaries, recording them photographically, and then calculating the area of each fraction by planimetry.

Zone electrophoresis[3] in immobilized media (filter paper strips, glass beads, starch, gels) has also been used as a separation method for proteins and substances of lower molecular weight. It has the advantage of providing a micromethod with a less expensive apparatus.[4, 5] Due to problems of adsorption of the protein with the media and the unequal combination of the staining dyes with the various protein fractions,[6] zone electrophoresis may achieve the precision of the "free" or moving boundary method[7, 8] with normal but not with pathologic sera. It has proved particularly valuable in the determination of substances that travel along or are bound to protein fractions such as lipoproteins,[9] mucoproteins,[10] vitamins,[11] enzymes,[12] hormones,[13] metals,[14] and types of hemoglobin.[15]

Clinical electrophoresis would not have progressed so rapidly without the pioneer work of Kurt G. Stern. At Yale University during the latter part of 1937 he constructed one of the first apparatus of the design of Tiselius. Later, he conceived the idea of folding the optical system by the use of mirrors, so that a smaller, compact apparatus resulted. This was tried out successfully in a pilot model that was used at Mount Sinai Hospital, New York City, for the study of about 1000 samples of

* The Medical Instruments Section will be featured in this journal during 1957. Outstanding authors have contributed articles to this series that will depict a panorama of the role of scientific instruments in clinical medicine.

normal and pathologic serum.[16] This was the prototype of the instrument shown in figure 1.

With this impetus, other compact apparatus was devised, such as the Perkin-Elmer,[17] the Kern,[18] and the Antweiler,[19] and the moving boundary method became a useful adjunct to an infinite variety of biochemical problems.

When the clinical field of electrophoresis was reviewed in 1946,[20] there were about 300 papers published, and according to a bibliography edited in 1955,[21] there were about 3000 papers listed in the field of human pathology. This article will not attempt to cover the entire subject, but will demonstrate changes of the protein spectrum in representative types of disease; moving boundary and zone electrophoresis experiments will be grouped together. References to many articles have been omitted due to lack of space rather than lack of merit. The fundamental work of L. G. Longsworth, D. H. Moore, Edwin Cohn, and the Harvard group are referred to in earlier review papers[20, 22–24] or books.[25–27]

NORMAL SERUM

Since there are so many variables and critical factors in the electrophoresis of proteins, it has been difficult to establish normal values. The type and strength of

FIG. 1. Aminco-Stern portable electrophoresis apparatus. (Courtesy of American Instrument Co., Silver Spring, Md.)

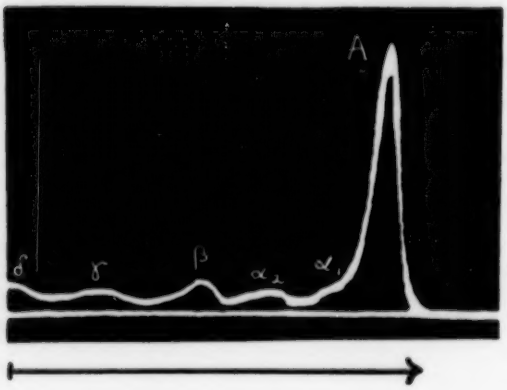


FIG. 2. Representative diagram of normal human serum,[16] recorded with slit diaphragm. Serum diluted with 2 volumes of diethylbarbiturate buffer, *p*H 8.6, ionic strength 0.1. Duration of experiment 8580 seconds at 1.9 C. and a potential gradient of 4.5 v./cm. Protein concentration 2.35 per cent. Explanation of symbols: α_1 = alpha$_1$ protein; α_2 = alpha$_2$ globulin; β = beta globulin; γ = gamma globulin; δ = stationary anomalous boundary, due to protein-buffer-salt gradient.

buffer, *p*H, temperature, method of measurement, amount of current, and innumerable technical details have influenced the results, but for human serum in clinical work there is now general agreement on employing a barbiturate buffer of *p*H 8.6, ionic strength 0.1, and on using results calculated from the ascending limb in the moving boundary method. The fastest moving boundary is albumin, and the α, β, and γ globulins are in decreasing order of mobility. The stationary delta boundary in the ascending limb and the corresponding epsilon boundary in the descending limb have been recognized as boundary anomalies, largely due to the transport of buffer ions by the proteins during electrophoresis. The β peak in the descending limb shows a peculiar spike, which may be due to a reflection phenomenon. The *relative percentages* of the serum protein are obtained by measurement with a planimeter of the total and fractional protein surface areas. *Absolute* protein values are computed by multiplying the total protein content of the serum (obtained from the Kjeldahl nitrogen or any other standard chemical procedure) by the relative figures. A representative pattern of normal serum protein is shown in figure 2.

ADULT NORMAL SERUM

The following table (table I) for normal sera was taken from Berry and Chanutin[28] with the addition of data from Gordon[29] and Dryer et al.[30]

A constancy in the electrophoretic patterns has been observed in a number of persons by Bernfeld et al.[34] In a comparison of 5 pair of brothers and a father and son, Berry and Chanutin[28] also found a similarity in the contours of the patterns.

In similar groups of Negroes and Caucasians, significantly higher mean concentrations of γ globulin were found in the Negroes.[35]

INFANCY AND CHILDHOOD

Lubschez[36] and Knapp and Routh[37] investigated the plasma proteins in healthy children and found that the mean values agreed well with results for normal adults. The percentage of albumin decreased from infancy to mid-childhood and appeared

to be lowest from 5 to 11 years, although the absolute figures showed no significant decrease. The alpha$_2$ globulins were highest in infancy and decreased gradually with increasing age. Gamma globulin decreased from unusually high levels in the newborn infant to unusually low values in infancy, then gradually increased with age (5 to 11 years) to reach the normal adult level.

In a study of 10 umbilical cord samples analyzed by paper electrophoresis[38] for proteins, lipoproteins, and glycoproteins, quantitative differences were found between newborn infants and adults in all categories.

NORMAL AGED SUBJECTS

The blood serum of 31 normal human subjects of ages ranging from 65 to 95 years has been examined.[39] The aged persons differed from younger subjects by having a lower albumin-globulin ratio and albumin concentration and a higher β globulin.

PREGNANCY

Detailed studies have been made of the plasma proteins during the reproductive cycle.[40, 41] In the first trimester of pregnancy only the decrease in γ globulin was significant. During the second trimester both the albumin and γ globulin were increased. Decreases in albumin and γ globulin and increases in fibrinogen and alpha$_2$ globulins were significant for the final trimester both in relation to the second trimester and to nonpregnant values. The return of the plasma proteins to normal was almost complete by 6 to 12 weeks post partum, and this seemed to be uninfluenced by lactation or its suppression, or the early re-establishment of menstruation.

In a study of the toxemias of pregnancy[42, 43] it was suggested that alterations in the plasma proteins represent a modification of changes that are physiologic in pregnancy. Deviations from normal in the third trimester of pregnancy may antedate the appearance of clinical signs and symptoms of toxemia. Changes in the urinary proteins have been studied by Parviainen et al.[44]

TABLE I

Mean Percentage Distribution of Normal Human Sera

No. sera	Albumin	Globulins				References
		Alpha$_1$	Alpha$_2$	Beta	Gamma	
46	60.6±3.5	4.0±0.6	9.2±1.5	14.0±1.6	12.4±2.7	Berry and Chanutin[25]
43	53.3±2.6	8.0±1.35	10.4±1.38	13.8±1.89	14.2±2.68	Seibert et al[32]
10	56.5±2.8	5.2±1.7	9.0±1.4	15.2±1.5	14.2±1.8	Cohen et al[21]
10	60.3±2.8	4.0±0.8	9.7±1.5	12.8±1.2	13.2±1.7	Sterling[33]
80	56.2±2.8	7.2±1.3	8.8±1.9	13.1±2.5	14.7±2.6	Reiner et al[16]
16	61.5±4.17	4.70±0.9	9.45±1.7	10.78±1.08	8.46±2.51	Dryer et al[20]
37	56.3±2.6	5.7±0.7	9.3±1.3	14.7±1.6	14.1±2.6	Gordon[29]

* This table was taken from Berry and Chanutin[25] with the addition of data from Gordon[29] and Dryer

STARVATION AND HYPOPROTEINEMIA IN NORMAL SUBJECTS AND SURGICAL PATIENTS

Ancel Keys[45] and his group studied the effect of starvation on the protein pattern of normal young men. There were no protein changes specifically characteristic of caloric undernutrition whether produced by complete or semistarvation. There is no valid evidence relating the decrease in albumin and increase in α globulins (observed in many acute and chronic diseases) to the protein deficiency of caloric undernutrition, which may accompany these diseases.

Elman[46] has pointed out that plasma volume must be taken into account for a proper evaluation of nutritional hypoproteinemia. Postoperative changes were found during the first four days in the majority of patients.[47] Prendergast and Fenichel[48] found that after major surgery, serum protein components were maintained when natural high protein foods were given. Williamson,[49] in a discussion of protein metabolism in wound healing, includes an extensive review of the literature.

NEOPLASTIC DISEASES

In *Hodgkin's disease* the protein patterns were nonspecific but seemed to be correlated with the clinical state of the patient.[50–53] *Lymphosarcoma* showed a lowered albumin and slightly raised α globulin and fibrinogen. In the patients with chronic *lymphatic* and *myelogenous leukemia*, the γ globulin was elevated.[51]

The changes in the plasma proteins that occur in neoplastic diseases are not specific except in certain types of *multiple myeloma* and will be discussed on page 385.

CONNECTIVE TISSUE DISEASES

Serum protein fractionation in collagen and rheumatic diseases has been investigated thoroughly.

In studies on the plasma of children with *rheumatic fever*, Wilson and Lubschez[54] found a prolonged elevation in the γ component after an antecedent respiratory illness, with or without the development of rheumatic fever; the α globulin components were usually elevated during the febrile periods. Routh et al[55] found in children that all serum components except β globulin were altered in the acute stage. As the disease regressed, the proteins returned to normal values. The inactive rheumatic patients seemed to be capable of normal protein metabolism.

In a zonal electrophoretic study of proteins in *rheumatoid arthritis* and *ankylosing spondylitis*, Hunt and Trew[56] found a moderate to marked rise in the relative fibrinogen and γ globulin levels, while the plasma albumin tends to be correspondingly reduced, with no significant change in the α and β globulins. Routh and Paul[57] found in general that the changes in albumin, alpha$_2$, and γ globulins and in fibrinogen are more marked in *rheumatoid arthritis* than in *rheumatic fever*. Laurell[58] and Reid et al[59] found abnormal components in the sera of patients with *rheumatoid arthritis*. A comparison of synovial fluid and serum proteins has been made by Perlmann et al[60] and Gaebler et al.[61]

Although the total protein content of the serum is generally within normal limits

in disseminated *lupus erythematosus*, the albumin fraction is decreased, the alpha$_2$ and γ globulins are increased, while the alpha$_1$ and β globulin fractions remain in the normal range.[62, 63] As the condition of the patient improves temporarily, either under treatment or during a spontaneous remission, the protein fractions will approach normal amounts,[63–66] with the alpha$_2$ globulin the last to decrease.[62] Typical patterns before and after treatment with corticoids are shown in figures 3 and 4.

The mechanism of the lupus erythematosus cell phenomenon has been studied by Haserick et al.[67] The metabolic actions and fate of corticoids in man has been investigated.[68, 69] The effects of nitrogen mustard therapy[70] and also of acetylsalicylic acid ingestion[71] have been studied.

Walker and Benditt,[72] in a study of serum proteins in connective tissue disease, found in subacute and acute disseminated *lupus erythematosus*, in diffuse *scleroderma*, and in *rheumatic fever* that there is a decrease in serum albumin and a γ globulin increase; in *dermatomyositis*, a decrease in albumin and total protein levels. In *peri-*

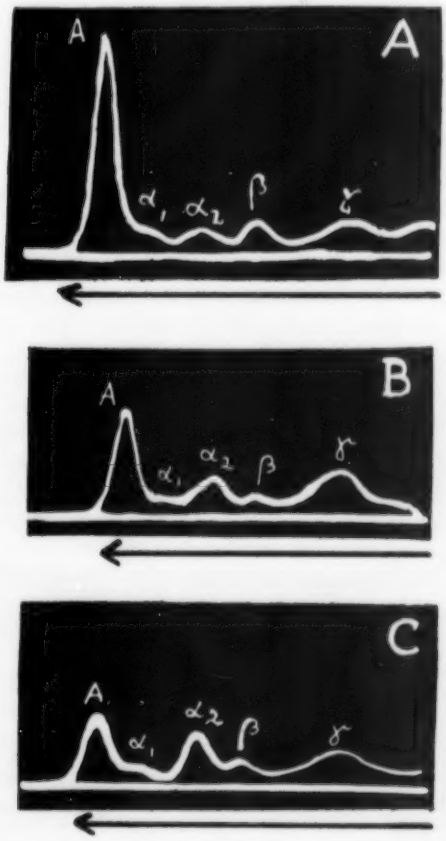


FIG. 3. Representative electrophoretic patterns of normal serum (*A*) and of two sera (*B* and *C*) from patients with *disseminated lupus erythematosus*.[66]

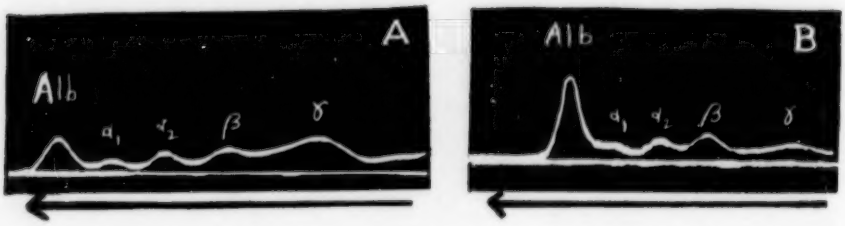


FIG. 4. Electrophoretic diagrams of the serum proteins of a patient with *disseminated lupus erythematosus* before (*A*) and after (*B*) therapy with cortisone and ACTH.[66]

arteritis nodosa[73] all fractions of the globulins are raised and the albumin level is decreased.

CARDIOVASCULAR SYSTEM

The changes in the protein spectrum in disorders of the cardiovascular system are not specific but depend on the underlying basic or inflammatory process. For example, in *endocarditis* there was an increase in α globulins but when sepsis was present there was a tremendous increase in γ globulin.[60, 74] In chronic *congestive heart failure*, uncomplicated by other factors, the albumin was decreased and the γ globulin was increased.[75]

ENDOCRINE DISEASES

The changes in the protein spectrum in endocrine disease are mostly nonspecific, and deviations from the normal are due largely to complications of other organic diseases. Studies of mucoproteins, glycoproteins, and lipoproteins associated with the protein fractions may shed more light on the nature of the disorders than the protein fractions per se. In untreated diabetes the total protein is normal with a decreased albumin and increased β globulin but with a return to normal when the disease is under control; when complicated with *retinitis* the proteins remain abnormal;[27] in *Kimmelstiel-Wilson* syndrome there was a hypoalbuminemia and a shift in the lipoproteins.[76]

The deviations from the normal protein pattern are not striking in either *hypo-* or *hyperthyroid* states.[52, 77] Plasma mucoproteins were elevated in *thyrotoxic* and low in *myxedematous* patients, but became normal in the euthyroid state.[78] The lipoproteins were increased in *myxedema* but decreased after treatment with *thyroxine*.[79]

A typical protein pattern was found in patients with adrenal cortical hyperactivity of pituitary origin—*Cushing's syndrome*; after hemiadrenalectomy the protein distribution gradually became more normal.[80] In hypoadrenal activity, as in *Addison's disease*,[81] the plasma albumin was decreased and the alpha$_2$ globulin fraction was below normal. One patient with acromegaly had a total protein, α, and γ globulins that were all below normal.[82]

RENAL DISEASES

In nephrosis there is a highly atypical serum pattern with an extremely low

albumin and γ globulin with an unresolved component in the α and β regions.[82–84] (See figure 5.) The urine of these patients yields a protein pattern similar to that of normal serum. The increase in the serum fractions has been shown to be due to lipoproteins.[76, 85] In patients successfully treated with ACTH, the protein defects were remedied;[86] the cholesterol reduction generally accompanied a reduction of the α and β globulins although the γ globulin did not rebuild completely.

In chronic *nephritis* the pattern differs little from normal except for a diminution of serum albumin and an increase in alpha$_2$ globulin. The metabolism of plasma proteins in the *nephrotic* syndrome has been studied in 6 children who were given tracer doses of radioiodinated human plasma albumin and γ globulin and later some were given iron-binding globulin. Except in 1 case, the rate of synthesis of these protein fractions was at the upper limit of normal.

LIVER DISEASE

Since the liver plays such a dominant role in the synthesis of plasma proteins, many dysfunctions of the organ are mirrored in changes in the various protein fractions. Severe strains on metabolism associated with many diseases may cause liver damage, e.g., *infectious mononucleosis*, *malaria*, *lobar pneumonia*, *typhoid fever*, various

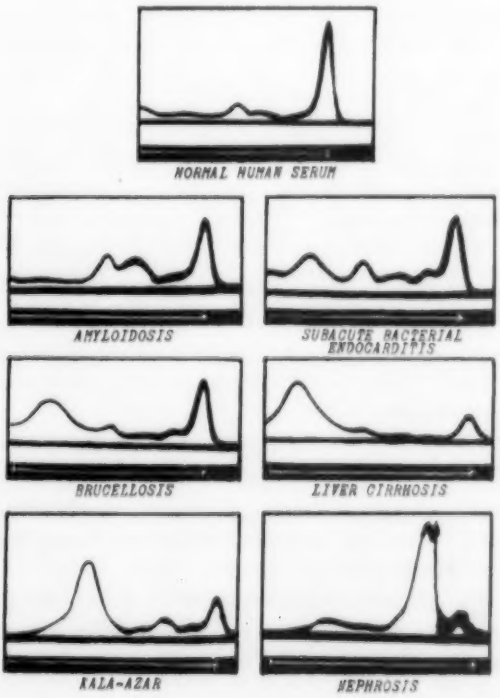


FIG. 5. Serum protein patterns in various types of disease.[116] Ascending boundaries, barbiturate buffer, *p*H 8.6.

anemias, *syphilis*, *cholera*, *diabetes*, and *thyrotoxicosis*; surgical operation and pregnancy may cause impairment of liver function in some patients. The total protein is often within normal limits so a true picture can be obtained only from detailed protein fractionation.[87]

Decreased albumin values are found in patients suffering from *cirrhosis*, in *viral hepatitis* (in clinically active stages), nutritional liver disease, and neoplastic disease involving the liver. The decrease in albumin is one of the factors in the flocculation tests of "liver function."[88–91] As the patient recovers, the albumin returns to the normal amount.

There is a tendency for lower α globulins as well as those substances associated with it, namely, mucoproteins, pseudocholinesterase, amylase, lipase, and esterase.[92] There has been some discussion as to the merits of mucoprotein determinations as a differential diagnostic aid.[92, 93]

Beta globulins are elevated in most hepatobiliary diseases, with the rise running parallel to the thymol turbidity *only* in cirrhosis with jaundice. Extra components not found in normal serum may appear in patients with liver disease.[94, 95]

Gamma globulins reach their greatest increase in some hepatitis patients, with a high concentration in cirrhosis in which jaundice was indicative of the activity of the process. In *hemolytic jaundice* the mean is in the normal range although in about 15 per cent of the cases it was exceeded.[96] The presence of infection failed to influence the γ globulin level. *Viral* and *toxic hepatitis* patients had elevated γ globulin levels, while in *cholangiolitic hepatitis* they were extremely high, and in *xanthomatous biliary cirrhosis* they were moderately elevated. There was no correlation between the γ globulin level and the presence of ascites or between the total serum bilirubin, total cholesterol, ester ratio, or thymol turbidity.[96]

Many investigations have been made of the correlation of the semiempirical flocculation and turbidity tests of "liver function" with changes in the individual protein fractions.[97] The tests of widespread use in the United States include the cephalin flocculation test of Hanger,[98] the thymol test of MacLagan,[99] and the zinc turbidity test of Kunkel.[100] The measurement of γ globulin by de la Huerga and Popper has also been used.[91] Wuhrmann and Wunderly[90] give detailed instructions for performing liver function tests and give comparative results in many cases. For further details, consult Saifer,[88] Wunderly and Wuhrmann,[89] Katz et al,[101] Spellberg et al,[102] Maher et al,[103] Hartmann,[104] Popper et al,[91, 96, 105] Kibrick and Clements,[106] and Strade et al.[107]

INFECTIOUS DISEASES

In acute infectious diseases the general type of response is a decrease in the albumin and a rise in the α fractions in the early stages of disease with a continuous increase of the γ fraction.

In *pulmonary tuberculosis*, Seibert et al[32] found that in patients with minimal disease the sera showed a decreased albumin and an elevated γ globulin, while in more advanced stages all the globulins became increased. Volk et al[108] reported an elevation of γ globulin in all patients with active pulmonary tuberculosis, including

those with minimal lesions; the increase is proportional to the severity of the disease and tends to return to normal limits when the tuberculosis is arrested. In children, the serum γ globulin level follows a characteristic curve,[109] rising early in the course of the disease and returning to normal during convalescence. The levels are lowest in *tuberculosis* of the *bone* and highest in *miliary tuberculosis* without meningitis and in *adenitis*.

Plasma from patients with *anterior poliomyelitis* had a decreased amount of albumin, with the α globulins and fibrinogen increased although γ globulins were decreased in all types of poliomyelitis.[110] Steigmann et al found no significant changes from the normal pattern.[111]

Syphilis cases in the untreated stage showed an elevation of the α globulins in the secondary and tertiary stages and an increase in γ globulins in all stages. After treatment, the serum protein pattern tended to return to normal.[112]

An increased total protein and a proportionally large increase in γ globulin were observed in sera from patients with *sarcoidosis*.[32]

Infectious mononucleosis revealed mainly a diminution of the albumin fraction and an elevation of the γ globulin.[113]

The serum from *typhus* patients showed a distinct reduction in albumin content with increases in alpha$_1$, β, and γ globulins and in fibrinogen.[114] The α globulins were increased in *meningitis* (bacillary).

Waldenström et al[115] found in *lymphogranuloma venereum* that the γ globulin peak was broad as well as increased in height; usually there is an increase in all globulin fractions.

TROPICAL DISEASES

In early cases of *kala azar* the protein changes are minimal, but as the disease progresses the usual picture of hyperproteinemia and hyperglobulinemia appears;[116] the degree of the change is usually proportional to the enlargement of the spleen.[117] In the presence of malnutrition and severe anemia, the usual protein increase does not occur. Changes are due to both chronic infection and associated liver dysfunction.[118] Abnormal components have been found both in the γ globulin fraction[119] and in one migrating faster than albumin.[114]

Leprosy shows a diminution in the albumin and some increase in the α and γ globulin fractions.[114]

HYPOGAMMAGLOBULINEMIA

There are apparently two types of hypogammaglobulinemia, one in which the absence of γ globulin is associated with lack of antibodies[120–122] and the other in which the patient has had infectious diseases only rarely in spite of the low γ globulin.[123] Bruton[120] found normal proteins with the absence of γ globulin in an 8 year old boy who had recurrent pneumococcal sepsis; after the monthly administration of γ globulin he remained free of such infections for a year.

The patient of Schick and Greenbaum[123] was followed by the author at Mount Sinai Hospital, New York City, for eight years. Innumerable electrophoretic serum

protein patterns were obtained after the administration of albumin, γ globulin, antiserum, ACTH, high protein and high amino acid diets. Any elevation of the γ globulin fraction was transient, although the patient stays unusually free of infections.

Bendich and Kabat,[124] by the quantitative precipitin method, followed the rate of elimination of transfused γ globulin from the blood stream of 2 patients with *idiopathic hypoproteinemia* and found that the half life of this fraction was three to four days. In a case of *acquired hypogammaglobulinemia*[121] in an adult with several chronic secondary infectious complications and a mediastinal mass, the infections could be controlled only with sulfadiazine and γ globulin therapy. The half life of administered γ globulin was approximately 36 days, and that of the six antibodies derived from the globulin varied from 15 to 75 days.

SKIN DISEASES

The dermatologic diseases show no characteristic pattern and usually only slight deviations from the normal patterns.[125] Serum protein changes are similar in both diffuse and localized *scleroderma*.[126] The total protein value is normal, with a decrease in the albumin and an increase in the γ globulin fraction.

Patients with acute *pemphigus vulgaris* had serum proteins with the albumin reduced to one-fourth and the α globulins increased in the later stages of the disease.[127]

MISCELLANEOUS

Allergic Diseases. Few changes in the protein pattern of common allergic diseases without complications are recorded, although antibodies can be identified in various globulin fractions.[128–132] In *chronic infective asthma* and intrinsic *dermatitis*, the serum proteins show abnormal distribution,[131] which appears to be related to the chronic underlying infection.

Multiple Sclerosis. The serum protein pattern found in most of the cases[132] was a significantly decreased albumin, normal alpha$_1$ globulin, increased alpha$_2$ and β globulins with a slightly elevated or normal γ globulin. In another series, Bernsohn and Cochrane[134] found an increase in the alpha$_2$ globulins with a heterogeneity characterized by a double peak in some instances and a concomitant reduction in the albumin. Kabat et al[135] found an increased γ globulin in the cerebrospinal fluid in the majority of patients. An increase in γ globulin hexose was found, which reflects the rise in γ globulin in spinal fluid.[136]

In a group of patients after brain operations, the total protein and albumin decreased and the globulins tended to increase. After ventriculograms and less drastic procedures in another group, there was little change in the total, but some alteration in the various protein fractions.

CEREBROSPINAL FLUID

There have been many recent studies of cerebrospinal fluid since only a small quantity of substance is required in paper electrophoresis analysis.[137–140] Kabat

et al,[135] after a simultaneous study of serum and spinal fluid, concluded that the spinal fluid γ globulin is derived partly from the blood and partly from tissues of the central nervous system. Schneider and Wallenius[141] found all the components normally present in serum. In some inflammatory diseases such as syphilis, they found increased amounts of α and β globulins. Hoch and Chanutin,[142] Aly,[143] and Bauer[144] have found components migrating faster than albumin. In diseases where increased permeability of the blood into the spinal fluid would be expected (such as inflammation of the meninges), a specific type of pattern was found. In acute nonpurulent *meningitis* there is an increase in the α and γ globulins with a corresponding decrease in the albumin fraction.[145]

HEMATOPOIETIC DISEASES

One of the outstanding contributions of electrophoresis to modern medicine has been in the study of hemoglobin. The discovery of an electrophoretically abnormal hemoglobin in *sickle cell* disease provided the first positive evidence that adult hemoglobin exists in more than one molecular form.[15, 146] In the majority of healthy individuals, fetal hemoglobin is no longer detectable after the first year but in certain chronic anemias the production may continue indefinitely.[147] In patients with sickle cell anemia an abnormal hemoglobin was found, which differs from normal in having more positive charges per molecule in the *p*H range 5.7 to 8.0. In sickle cell trait, not associated with the anemia, both the normal and abnormal hemoglobin were found in the same erythrocytes. According to a late report[148] there are now 10 abnormal human hemoglobins that differ in their physicochemical properties. The majority of a series of patients with sickle cell anemia[149] showed decreased albumin, elevated γ globulin and fibrinogen. This may represent the reaction to tissue breakdown caused by the sickling process in various organs.

Normal hemoglobin has been found in patients with *paroxysmal nocturnal hemoglobinuria*.[150, 151] An electrophoretic anomaly called alpha$_x$ globulin has been found in the plasma of *hemophiliacs* and in members of their families who are not active bleeders.[152]

The leukemic states are associated with a diminution in the absolute amount of albumin and a rise in the α globulins. Gamma globulin values, both absolute and relative, were elevated in *monocytic leukemia*, reticulum cell *sarcoma*, and infectious *mononucleosis*, while they were decreased in chronic *lymphocytic leukemia*.

One of the most interesting diseases from the standpoint of protein studies is *multiple myeloma*. In about 80 per cent of the cases,[153] one of the normal globulin fractions is replaced or encompassed by an anomalous protein fraction, which has approximately the same mobility and usually can be distinguished by its sharp peak in an electrophoretic diagram (see figure 6). The amount of albumin usually decreases with the increase in the anomalous fraction. There is a remarkable variability to the protein patterns with little or no correlation with the chemical and histologic findings and the clinical symptoms.

The migration of the anomalous fraction may be slower than, equal to, or intermediate between normal serum components. In a series of 91 patients studied,[153]

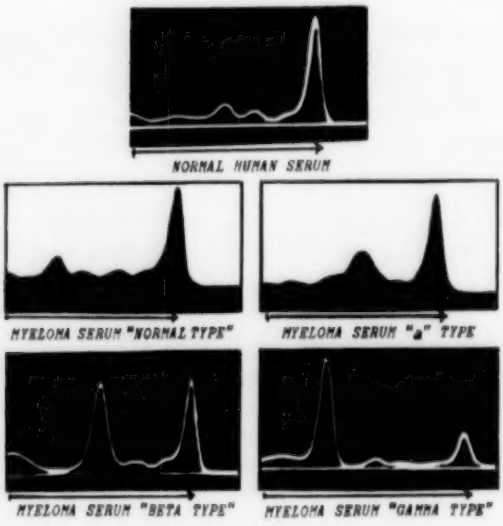


FIG. 6. Serum protein patterns from patients with *multiple myeloma*.[153]

the average total serum protein was increased. Twenty-two per cent of these patients showed only minor anomalies, 6.6 per cent revealed an abnormal component in the range of α globulins, 15.4 per cent showed major peaks in the β region, and 55 per cent disclosed abnormal components in the γ globulin region. For a detailed discussion of the clinical history and treatment of the majority of these patients see Snapper et al.[154] Impairment of renal function is a frequent and serious complication and may alter the protein distribution in the serum to some degree and may account for the occasional appearance of albumin and other fractions in addition to Bence Jones protein, which appears in 40 to 50 per cent of the cases. Virtually normal electrophoretic patterns have been found in the serum from many patients who excrete large amounts of Bence Jones protein in the urine.

The wide variation in the characterization of the Bence Jones protein is due partly to the multiplicity of procedures used for isolation but is mostly due to qualitative differences in the protein itself. Putnam and Miyake[155] analyzed Bence Jones proteins and found that none were identical in all the physical properties studied—sedimentation constant, diffusion constant, isoelectric point, *p*H, mobility curve, and stability. The N-terminal amino acid analysis showed differences in chemical structure as well.

Isotopic study of plasma protein formation in a patient with multiple myeloma has failed to reveal any relationship in the synthesis of a heterogeneous, abnormal β globulin and a urinary Bence Jones protein.[156] No evidence was found for the origin of urinary Bence Jones protein from the plasma cryoglobulin in a subject who was given N^{15}-labeled glycine.[157] In another patient[158] the rate of protein synthesis and the size of the metabolic pool was estimated as normal by N^{15}-labeled glycine.

The immunologic characteristics of Bence Jones proteins suggest that they may be portions of normal serum protein molecules or altered γ globulins.[159]

An atypical electrophoretic peak in the region of alpha$_2$ and β globulin was found in the serum of 5 related patients with familial primary systemic *amyloidosis*.[160]

SUMMARY

Since most diseases display many symptoms reflecting multiple tissue and organ involvement, it is not surprising that each disease does not produce a specific protein picture. In general, when the serum protein fractions are in abnormal distribution, the albumin is diminished and the globulins are increased. Serum *albumin* is decreased when there is an inadequate protein intake, excessive loss of protein, or lack of synthesis. The excessive loss of protein may be due to such conditions as *nephrosis*, recurrent *hemorrhage*, exudation of serum, massive chronic *suppuration*, severe *burns*, and repeated abdominal *paracenteses*. There may be a lack of albumin synthesis in *nephrosis*, *liver diseases*, and *cachexia*.

Alpha globulins are increased in acute febrile conditions such as *lobar pneumonia*, acute *rheumatic fever*, and *tuberculosis* and in *lupus erythematosus*, *periarteritis nodosa*, *nephritis*, *rheumatoid arthritis*, *leprosy*, *sarcoid*, *carcinoma*, *Cushing's syndrome*, and sometimes in *thyroid disease*, *diabetes*, *Addison's disease*, liver disease, and pregnancy.

Beta globulins show the greatest increase in *nephrosis* and acute *hepatitis*, but may also show varying increments in malignant *hypertension*, *periarteritis*, *nephritis*, *liver diseases*, chronic *infections*, *tuberculosis*, *sarcoid*, *hypothyroidism*, *Cushing's syndrome*, and some types of *diabetes*.

Gamma globulins are increased in infectious and hypersensitive and miscellaneous states such as *lymphogranuloma venereum*, *syphilis*, *leprosy*, *kala azar*, *lupus erythematosus*, *periarteritis nodosa*, *rheumatoid arthritis*, subacute bacterial *endocarditis*, *rheumatic fever*, *tuberculosis*, *sarcoid*, and acute and chronic *infections*. There may also be an increase in neoplastic disease such as *lymphoma* and *leukemia*. *Liver* disease will cause an increment in the γ globulin fractions, with *cirrhosis* usually producing a greater change than *hepatitis*.

The protein pattern in *multiple myeloma* may deviate slightly from the normal or may show an anomalous protein fraction at any point in the globulin spectrum.

Medically, electrophoresis may be of greater assistance in following progressive protein changes during the course of the disease rather than in its diagnosis. However, it has led to the continuous improvement of methods of protein fractionation. In combination with other physical and chemical methods, knowledge has been gained as to the protein size, shape, and charge, to the amino acid composition (with the development of isotope tracers) and their place in metabolic body processes, the quantitative interaction as with antigens and antibodies, and substances associated with proteins, such as carbohydrates, lipids, hormones, vitamins, and metals.

(Please turn to page 398 for Bibliography.)

Reduce and Stay Reduced. NORMAN JOLLIFFE. New York, Simon and Schuster, 2nd ed., 1957. Pp. 266. $3.50.

A salutary corrective for many popular misconceptions about the causes of overweight, methods of dieting, and techniques of maintaining a reduced weight is this practical and authoritative book on why and how to reduce. According to Dr. Jolliffe, the essential factor in attaining and maintaining a proper weight is the regulation of the "appestat," the mechanism located in the hypothalamus that controls the desire for food.

Part one of the book describes the functions and disorders of the appestat, catalogues the main causes of a too-high appestat as habitual, cortical (purposeful), and psychosomatic, and explains why no reducing diet will be successful unless it also reduces the level of the appestat to the point where the reducer can reach satiety on a lowered food intake. Also in this section are chapters describing the reasons, indications, and contraindications for reducing; the basic physiologic principles of metabolism, including the factors of physical activity, temperature, and energy and water balance; and the mathematics of gaining and losing weight.

Devoted to practical and specific dietary plans, part two gives useful information on selecting the diet, food values and their use, the diet pattern and menu plans and how to modify them, and the principles of reduced cookery. Also included are 66 complete daily diets, a list of common foods and their calorie counts, and 49 pages of reducing recipes. A lover of good food, Dr. Jolliffe has no patience with the bland unpalatable fare so often met with in reducing diets and many of his recipes, particularly those that are salt-free, depend heavily on the use of herbs for seasoning.

For those who may be interested, an appendix elaborates on certain statements in the text concerning physiology and body chemistry in obesity, some of the metabolic and endocrine gland diseases associated with disturbances in weight, and the functions of the endocrine glands as they affect weight in health and disease.

New in this second edition are a heart-saver diet for normal adults, salt-free and low-sodium diets, an "emergency liquid formula," indexes, and revisions in the diets and recipes so that all obtain less than 30 per cent of their calories from fat.

Although this book is intended primarily for the layman who wishes to reduce, it will also be of interest to the physician faced with the problem of prescribing and supervising the diets of his obese patients.

Illustrated Medical and Health Encyclopedia. MORRIS FISHBEIN, Editor. New York, H. S. Stuttman Co., 1957. 4 Vol. Pp. 2166. $19.50.

Probably the most thoroughgoing and authoritative source of current medical information for the layman is this richly illustrated and moderately priced four-volume encyclopedia. Prepared by the former editor of the *Journal of the American Medical Association* and 29 collaborators in various medical and surgical specialties, the book covers all the major ills that flesh is heir to and ranges widely over many of the rarer diseases as well.

Technical terms, particularly those peculiar to specialties, have been avoided as

far as possible. Symptoms are described in such a way as to discourage self-diagnosis, but the causes and the anatomic and physiologic aspects of disease are dealt with carefully and clearly. Although well-established therapies are described in broad terms, dosages are not given and mutilating operations such as amputation not detailed. On such controversial subjects as the relationship between smoking and lung cancer, a temperate view is adopted, and as far as is possible all recognized opinions as to causes and treatment of disease are presented.

The alphabetically arranged, heavily cross-referenced entries are amplified and correlated by 32 special articles written by Dr. Fishbein or by his collaborators. These include articles on each of the body systems, on special organs (such as eye, ear, heart, kidney, and skin), and on areas and developments in medicine that recently have stimulated more than ordinary interest (nervous and mental disorders, diet and nutrition, occupational diseases, diseases of old age, and stress in relation to disease). Emphasized also are those disorders that loom large and threateningly on lay horizons or those concerning which the public needs to be educated: heart disease, diabetes, allergy, cancer, tuberculosis, and transmissible and venereal diseases. Articles on first aid, choice of a physician, and the contents of the family medicine chest are of immediate practical value. The medical and psychologic aspects of human mating and reproduction, from the earliest sex education of the child, are covered by articles on sex hygiene, hygiene of women, pre- and postpartum care, and care and feeding of the child, as well as by many related entries.

The illustrations—photographs, line drawings, colored plates, and charts—maintain the standards set by the text in variety and detail, and there are a surprising number of illustrations of laboratory procedures and equipment. It is unfortunate that more attention was not paid to mechanical production details, as many typographic errors and some editorial oversights mar the text. Barring these minor flaws, however, the encyclopedia should be a useful and frequently consulted adjunct to the family medicine chest. Whether it will reduce the number of questions now asked the family physician or create a barrage of new ones remains to be seen.

A Glossary of Mycology. WALTER H. SNELL AND ESTHER A. DICK. Harvard University Press, Cambridge, Mass. 1957. xxxi + 171 pp. Illustrations by Henry A. C. Jackson. Price $5.00.

This dictionary, which defines nearly 7000 terms, more than doubles the content of its predecessor, *Three Thousand Mycological Terms*. Words used in medical mycology and the field of antibiotics are defined. In many cases, the discoverers of substances or originators of terms are given. Some fault can be found with the coverage of antibiotics. Although incompleteness is understandable, some very important antibiotics have been omitted. For example, erythromycin, fumagillin, and tetracycline are conspicuous by their absence, as are the antifungal agents ascosin, candicidin, and fungicidin (nystatin). Chloramphenicol, chlortetracycline, and oxytetracycline are listed under their trade names, while the proper generic names just mentioned have been omitted. Very clear diagrammatic illustrations are given for 191 terms. This glossary is a valuable reference book for every mycologist and many workers in allied fields of industry and experimentation.

ADVANCED REPORTS FROM CURRENT MEDICAL MEETINGS

This section of the INTERNATIONAL RECORD OF MEDICINE features reports on papers delivered at current medical meetings in the United States and abroad.

Case Experiences in Thyroid Disease

Boston.—Diagnostic and therapeutic procedures in some fairly typical instances of thyroid disease are reviewed by Earle M. Chapman (Harvard Medical School and Massachusetts General Hospital, Boston). Although no diagnostic difficulties are expected in a representative case of Graves' disease, it was pointed out that the protein-bound iodine of the serum and the radioactive iodine uptake by the thyroid are superior to the basal metabolic rate determination, as tests of thyroid function. The protein-bound iodine determination plus the radioactive iodine uptake are 90 per cent accurate in combination. The basal metabolic rate is 75 to 80 per cent accurate.

In the treatment of uncomplicated cases of Graves' disease, drugs such as propylthiouracil and methimazole may be of use when the thyroid gland is relatively small. It was stressed that these medications should be continued for at least two to three months for a fair trial. Nevertheless, there is a 50 per cent chance of recurrence after stopping the drug up to one year after this therapy. Subtotal thyroidectomy is a valuable procedure, but complications of the operation and recurrence may occur in 3 to 5 per cent of operated cases. Therapeutic doses of radioactive iodine were regarded as the treatment of choice for middle-aged patients with Graves' disease. Objections to the use of the isotope seem to be invalidated by such statistics as have accumulated at the Massachusetts General Hospital. Not one case of carcinoma could be attributed to the radioactive iodine in a thousand cases so treated. Furthermore, there was nothing to indicate injury to testicular or ovarian tissues. Children born of male or female patients treated with radioactive iodine have not been shown to be adversely affected by this therapy. On the other hand, middle-aged patients with multinodular goiter and mild hyperthyroidism, often with accompanying heart failure and atrial fibrillation, benefit more from subtotal thyroidectomy. Nodular goiters respond poorly to treatment with radioactive iodine.

The problem of the patient with a solitary firm thyroid nodule is discussed. Dr. Chapman states that there is a 10 per cent chance of malignancy in such a lesion. A low radioactive iodine uptake in such a nodule suggests malignancy. Seventy-five per cent of such malignancies are operable with a good prognosis. Of the 25 per cent inoperable cases, three-fifths reveal differentiated cytology. The treatment of these patients involves ablation of the thyroid glands if the tumor takes up iodine, the use of a large treatment dose of radioactive iodine, and finally the use of substitution thyroid therapy two weeks after isotope treatment to suppress pituitary release of thyroid-stimulating hormone.

The diagnosis of thyroid carcinoma depends on a high index of suspicion. Skeletal and chest roentgenograms, together with direct counting of the radioactive iodine uptake, may assist in the diagnosis. A preoperative tracer dose of 500 to 1000 μc. of the isotope should be administered, and radioautograph and other histologic studies should be performed on the excised tissue. Postoperative tracer studies of metastases should be performed.

However, the best treatment of thyroid carcinoma is widespread and early surgery. Twenty patients with metastatic thyroid cancer were treated with radioactive iodine

out of 200 cases of metastatic thyroid cancer at the Massachusetts General Hospital. Ten of these patients are still living and well.

(Presented before the Spring Clinical Assembly, Massachusetts Chapter, American Academy of General Practice, Boston, April 28, 1957.)

The Combined Use of Antibiotic Agents

Philadelphia.—A symposium on the combined use of antibiotic agents was conducted with the following panel members: Gladys L. Hobby (Chas. Pfizer & Co.), Harrison F. Flippin (University of Pennsylvania), Earle H. Spaulding (Temple University School of Medicine), and Robert I. Wise (Jefferson Medical College). Supporters of antibiotic combinations claim that the emergence of resistant strains is decreased, synergism occurs, a wider spectrum is provided, and toxic agents may be safely used in lower doses. Opponents claim that evidence for these statements is meager, being available only for specific infections and for in vitro or animal experiments. Dr. Wise urges especially that fixed antibiotic combinations, such as are becoming increasingly available commercially, have great disadvantages: (1) They cannot be suited to the various situations encountered, as the antibiotic ratio is fixed. (2) Since the individual drug dose cannot be increased without increasing the amount of both drugs, a toxic or sensitivity-producing drug might have to be increased. (3) Inadequate doses of both antibiotics are frequently used, thus increasing the emergence of resistant strains to both drugs. This is exemplified by a tetracycline-oleandomycin combination available, which is claimed to be effective against resistant staphylococci. Seventy-five per cent of hospital staphylococci are resistant to tetracycline, especially in the low dosage provided. Only the oleandomycin is good for the recommended purpose, and even here, the dosage is too small. (4) False security is given to the practitioner, who is led to believe he has a highly effective agent. Sloppy diagnosis is thus encouraged.

General agreement was reached on the use of combinations in certain indications. In tuberculosis, almost any combination of effective drugs prevents resistance and should be used. In brucellosis, effective combinations are streptomycin with sulfadiazine, and clortetracycline with dihydrostreptomycin. Even here there is some controversy: chlortetracycline alone may be just as good. Subacute bacterial endocarditis frequently is caused by resistant organisms, and large doses of combinations are vital. *Streptococcus faecalis* is an example. *Staphylococcus* septicemia usually requires combinations in high doses to combat the all too common resistance; laboratory studies cannot be waited for.

In preoperative preparation of the intestine, combinations are needed to suppress the many species of bacteria. Combinations increase the risk of hypersensitivity reactions, and this is especially important with broad-spectrum antibiotics in bowel preparation, as the reactions often affect the bowel. Infections known to be due to large varieties of bacteria may be treated with combinations before laboratory studies separate out all the types involved. These infections would include contaminated burns and peritonitis. In trachoma, oxytetracycline and penicillin are often used, the first for the virus and the second for the bacterial component.

All speakers agreed that the use of combinations should be based on a good knowledge of the drug actions and, whenever possible, of the bacteria involved, rather than on empiric "shotgun" attempts or drug company propaganda.

(Presented before the Eastern Pennsylvania Chapter, Society of American Bacteriologists, Philadelphia, April 23, 1957.)

Neonatal Estrogen Excretion and Its Relation to Postnatal Weight Loss

London, England.—The excretion of estrone, estriol, and estradiol was measured by chromatography in the urine of neonates by Bruno Gans (Pediatrician, Miller General

Hospital, Greenwich, London) and John C. Thompson (Biochemist). They state that total estrogen excretion runs parallel with the loss in weight that occurs in the neonatal period. There is a particularly high concentration of estriol in the urine during the first few days of life. The 17-hydroxyketosteroids show little fluctuation and are unrelated to neonatal loss in weight. Gans and Thompson state that, in pregnancy, water retention is due to the presence of excess estrogens. They argue, therefore, that loss of estrogens in the neonate causes the loss in weight in the first week or so of life. Some loss of weight occurs, they say, when the infant catabolizes its own proteins, but they consider that the bulk of the loss is due to the elimination of the excess water that the infant has been storing since birth. The fetus is hydrated *in utero* because of the effect of the water-retaining estrogens secreted by the mother. After birth, the estrogens circulating in the infant are slowly excreted in the urine, with resulting loss of water and weight by diuresis. Gans and Thompson believe that the postnatal loss in weight is largely due to water loss. The maternal estrogen is probably destroyed in the liver of the newborn infant.

(Presented before the Royal Society of Medicine Section of Pediatrics, London, England, April 26, 1957.)

No Harmless Dose of Radiation

Washington, D. C.—Experts now have turned to the view that there is no such thing as a completely harmless dose of radiation, points out Walter D. Claus (Division of Biology and Medicine, Atomic Energy Commission, Washington). In a sense, the "maximum permissible dose rate" is a philosophic concept rather than a scientific one. It represents, he suggests, an estimate of what people could afford to pay, in terms of potential personal damage, for the benefits that could be obtained from x rays and gamma rays.

"Because of limited radiologic experience," Claus says, "it is necessary to assume that any practical limit on personnel exposure that may be set up today (such as the 0.3 r/week under which we have been operating) will involve some small risk of possible harm." In addition to bodily injury and the possibility of premature aging and shortening of the lifespan, Claus points out, there is the fear that even low levels of radiation will cause genetic damage. He says it was primarily because of the genetic consideration that the National Committee on Radiation Protection and three other groups reduced their prevailing recommendations for maximum permissible exposure.

The Atomic Energy Commission is considering the proposed reductions, which call for little or no change in occupational exposure rates to individual organs, excepting the gonads, but would cut by a factor of three the permissible exposure to the whole body and the gonads, limit the lifetime accumulation of dose, and impose severe limitations on average exposure to the general populace.

(Presented before the Industrial Health Conference, St. Louis, April 20–26, 1957.)

The Possibility of Diagnosis of Early Atherosclerosis

Warsaw, Poland.—Serum lipids, coagulation factors, and serum proteins in early and late phases of atherosclerosis were studied by E. Szczeklik, M. Orlovski, A. Janiakowa, and B. Bogdanikowa (Warsaw, Poland). Results were as follows. The free cholesterol was elevated even in the early phases, and in the late phases the elevation was more marked. In the early phases, there was no change in the cholesterol : phospholipids ratio. The changes were observed only in the late phases. In the early stages, an elevated prothrombin level, because of elevation of factor VII accelerator, and other changes occurred. All changes in coagulation mechanisms were more marked in the late phases of atherosclerosis, especially in myocardial infarction. In the early phases, plasma protein electrophoresis gave the normal pattern. The most marked elevation of lipids and

coagulation factor abnormalities could be found in atherosclerotic persons in the age group of 40 to 50.

(Presented before the Second Congress of Yugoslavian Cardiologists, Milocer-Budva, Yugoslavia, April 20–24, 1957.)

Fluorides and Fluorosis

Portland, Ore.—Although fluoridation of water supplies has focused attention on fluoride compounds, it is not so widely realized that they are used increasingly in industry also, says Merl M. Margason (Clinical Professor of Medicine, University of Oregon Medical School, Portland, Ore.). Because of these uses, the physician should be informed of the benefits and hazards of these substances.

Not all instances of industrial fluorine poisoning are due to chronic fluorosis. Dichlorodifluoromethane, a refrigerant gas, may cause unconsciousness if inhaled in a high concentration. Hydrogen fluoride, or hydrofluoric acid, is corrosive and, when inhaled, may cause death from pulmonary edema. It is possible that hydrofluoric acid accounts for some of the irritating qualities of smog. Tetrafluorethylene, an inert plastic, when heated as it is being machined, produces decomposition products that, inhaled, cause "plastic fume fever." The recently developed and now widely used low hydrogen-coated electrodes for arc welding also contain fluorine in the coating, which can be inhaled by the welder.

Chief sources of atmospheric pollution are the use of fluorspar (calcium fluoride) in the manufacture of iron and steel and cryolite (sodium aluminum fluoride) in the manufacture of aluminum. Depending on the rainfall and prevailing winds, the fallout may contaminate leaves of plants or grain used as forage by animals. It would appear, however, that considerable amounts of fluorine must be absorbed, or that renal impairment must alter the rate of excretion, for toxic symptoms to be produced. Some years ago, McClure et al found that when healthy young men were given between 4.0 and 5.0 mg. of fluorine daily, excretion was complete in the sweat and urine. Dr. Margason has had the opportunity to examine 18 employees of an aluminum company at yearly intervals for a total of 53 examinations. They had been in this industry from 1 to 30 years, and actual time spent on the "pot line" varied from less than 10 per cent to 90 per cent of the working day. Thorough examination of these men has revealed no symptoms or laboratory or roentgenographic evidence of changes that could be ascribed to fluorosis.

(Presented at the American College of Physicians, Post-Convention Tour, Puerto Rico, April 15, 1957.)

Arterial Damage and Metabolic Disturbance in Presenile Arteriosclerosis

Florence, Italy.—There are two stages of arterial change occurring in the latter part of life: atheromasia between the ages of approximately 50 and 70 and true arteriosclerosis thereafter, reports Enrico Greppi (Chief of Medical Service, University Hospital, Florence, Italy). Arteriosclerosis is a degenerative disorder, characterized by diffuse sclerotic changes in the walls of the peripheral arteries and certain biochemical changes in the blood; these biochemical changes also occur with the previous stage of atheromasia, though they are less pronounced than in arteriosclerosis. Atheromasia is characterized by lipoprotein infiltration of the intima of the large and medium arteries, especially of heart, head, and extremities, and by certain biochemical changes, which are due to hormonal disregulation, while the additional anatomic changes of arteriosclerosis are to be explained by the wear and tear of a long life.

Concerning biochemical changes of atheromasia, cholesteremia and changes of lipid metabolism are familiar, and we also know that coagulation time is shortened and prothrombin level is raised, as is heparin tolerance. Recent work carried out by Professor Greppi's co-workers, Antonini and

Salvini, dealing with the mucopolysaccharides of the blood, throws additional light on the thrombotic tendency of atheromasia. The level of the glycoproteins and of glucosamine was determined, showing that the polysaccharide level is definitely raised. The level of the heparinoid substances, which also belong in the chemical group of the mucopolysaccharides, is lowered in atheromasia and arteriosclerosis. Apart from these biochemical changes, the functional burden of hypertension developing in old age is a causative factor in the development of arteriosclerosis. Therapy consists of a low-fat diet, heparin in the dosage suggested by Gibson, hormones, iodine, and balneotherapy.

(Presented at the Postgraduate Geriatric Course, Austrian Geriatric Society, Bad Hofgastein, Austria, April 13–20, 1957.)

Rumination: A Psychosomatic Syndrome

Syracuse, N. Y.—A long known, but generally forgotten, psychiatric disorder of infants—rumination—is called to attention by Julius B. Richmond and Evelyn Eddy (Department of Pediatrics, State University of New York, Syracuse). Rumination consists of regurgitation of swallowed food with an effort to rechew the food. Dr. Richmond observed 4 cases, all of which developed after the fourth month of life, in bottle-fed infants. In all cases, the infants exhibited other manifestations of psychopathology, such as autistic play, purposeless movements, feces manipulation, withdrawal. All the mothers were found to have severe psychopathology, rendering them unable to "mother" their babies. These are dependent, immature women unable to satisfy their own needs, much less to provide love and attention to their children.

Dr. Richmond proposes that rumination may be the infant's attempt to replace the missing mother-love with the next most pleasurable act, i.e., eating. In doing this, the process of rumination becomes continuous (as long as the infant is left alone), and the child actually becomes malnourished. Herein lies the importance of recognizing this syndrome, since the patients under study were originally thought to have adrenal insufficiency, celiac syndrome, habitual vomiting, or other disorders. Hospitalization reverses the infant behavior and restores the mother's confidence in herself to the point that there is no recurrence after discharge from the hospital.

(Presented at the Regional Research Meeting, American Psychiatric Association, Syracuse, N. Y., April 5-6, 1957.)

Organized Enzyme Systems: Mitochondria

Madison, Wis.—Mitochondria as examples of complete enzymatic units containing all the enzymes and cofactors necessary for oxidation, none of which are unrelated, were discussed by David E. Green (Institute for Enzyme Research, University of Wisconsin, Madison). He discussed how these substances are arranged and how they function. The methods employed were those of classic analytic biochemistry and differential centrifugation.

Mitochondria can be prepared in quantities of about 100 Gm. a day from beef heart. By differential centrifugation they can be fragmented into a heavy and a light fraction. Electron microscopy shows the heavy fraction to consist of the mitochondrial cristae (the folded inner portion) and the light fraction to consist of the membranous envelopes surrounding the mitochondria. By chemical analysis the light fraction is found to contain flavin, heme, iron, copper, lipid, and cytochromes A, B, and C_1. The hemes from all three of these cytochromes can be reduced by electrons from either succinate or DPNH.

It is striking that the light mitochondrial fraction prepared from bacteria has the same properties and composition as that from beef heart. Extraction of the light fraction with acetone, under the proper

conditions, yields soluble succinic dehydrogenase, containing 1 molecule of flavin for each 2 of iron. Extraction with 9 per cent alcohol will yield soluble DPNH dehydrogenase with the same proportion of flavin to iron. These two enzymes are present in equal amounts. In the process of oxidation, electrons are taken up by these enzymes (which, of course, are specific for their own substrates). From then on, Dr. Green believes, the electrons are handled by a common pool of cytochromes and other enzymes. Cytochrome A is believed to be the link from cytochromes B and C_1 to molecular oxygen.

Also present in the mitochondrial chain of enzymes are lipid materials, including phospholipids, neutral fats, cholesterols, and a quinone. If this quinone is removed by extraction with heptane, the light fraction is rendered incapable of oxidizing succinate until enzymatic amounts of the quinone are added back. Dr. Green states that cytochrome C_1 can be converted with a lipid. He also expresses the opinion that lipids may compose the "crosslinks" connecting the chains of enzymes in the mitochondria.

Dr. Green plans to analyze other mitochondrial fractions using similar techniques. He hopes eventually to establish all the links in the oxidative chain, which is the basic mechanism for producing energy for all biologic processes.

(Presented as the Eighth Harvey Lecture before the Harvey Society of the New York Academy of Medicine, New York City, April 11, 1957.)

A "Pregnancy" of Five Years' Duration

Rotterdam, The Netherlands.—In 1951 a woman was sent to the hospital when it was found that she was pregnant and the unborn child was dead, reports Rudolf F. v. Wering (Director of School for Midwives, Rotterdam). Since injections of pituitrin had no effect, she was discharged from the hospital after a few days, undelivered. The patient was seen again five years later in a surgical department for a tumor in the abdomen. Roentgenograms disclosed a fetal skeleton. During laparotomy a lithopedion was extracted that lay free between the small bowels; there were no adhesions and no placenta. The patient told the physician that shortly after she left the hospital in 1951, menstruation returned, so that she forgot all about the pregnancy! It is possible that the intensely positive Wassermann reaction gives a better explanation for this forgetfulness, says Dr. Wering.

(Presented at the Joint Meeting of the Netherlands Gynecologic Society and the Belgian Gynecologic Society, Utrecht, The Netherlands, April 13, 1957.)

Progress in the Treatment of Hepatic Coma

Boston.—The current treatment of hepatic coma and its effectiveness at the Boston City Hospital are discussed by Charles Davidson (Associate Professor of Medicine, Harvard University, and Associate Director, Medical Service, Boston City Hospital, Boston). The usual case at this institution is the end result of alcoholic cirrhosis of the liver. The regimen for hepatic coma that has seemed most effective at the Boston City Hospital is as follows: dietary protein withdrawal; administration of oral antibiotics, particularly neomycin; the prompt control of gastrointestinal hemorrhage; the possible use of enema and purge to facilitate removal of protein from the intestinal tract.

With the possible exception of glucose administration, other methods of treatment of hepatic coma recently advocated have not proved valuable. These include the use of glutamate, arginine, and cortisone. Although glutamate and arginine may lower blood ammonia levels, their clinical value has been quite limited. Although ammonia intoxication is probably closely tied in with the clinical manifestations of hepatic coma, there is poor correlation of the arterial or venous ammonia levels with the clinical manifestations of hepatic coma. Furthermore, the rationale for the administration of glutamate and arginine is unclear at the

Salvini, dealing with the mucopolysaccharides of the blood, throws additional light on the thrombotic tendency of atheromasia. The level of the glycoproteins and of glucosamine was determined, showing that the polysaccharide level is definitely raised. The level of the heparinoid substances, which also belong in the chemical group of the mucopolysaccharides, is lowered in atheromasia and arteriosclerosis. Apart from these biochemical changes, the functional burden of hypertension developing in old age is a causative factor in the development of arteriosclerosis. Therapy consists of a low-fat diet, heparin in the dosage suggested by Gibson, hormones, iodine, and balneotherapy.

(Presented at the Postgraduate Geriatric Course, Austrian Geriatric Society, Bad Hofgastein, Austria, April 13–20, 1957.)

Rumination: A Psychosomatic Syndrome

Syracuse, N. Y.—A long known, but generally forgotten, psychiatric disorder of infants—rumination—is called to attention by Julius B. Richmond and Evelyn Eddy (Department of Pediatrics, State University of New York, Syracuse). Rumination consists of regurgitation of swallowed food with an effort to rechew the food. Dr. Richmond observed 4 cases, all of which developed after the fourth month of life, in bottle-fed infants. In all cases, the infants exhibited other manifestations of psychopathology, such as autistic play, purposeless movements, feces manipulation, withdrawal. All the mothers were found to have severe psychopathology, rendering them unable to "mother" their babies. These are dependent, immature women unable to satisfy their own needs, much less to provide love and attention to their children.

Dr. Richmond proposes that rumination may be the infant's attempt to replace the missing mother-love with the next most pleasurable act, i.e., eating. In doing this, the process of rumination becomes continuous (as long as the infant is left alone), and the child actually becomes malnourished. Herein lies the importance of recognizing this syndrome, since the patients under study were originally thought to have adrenal insufficiency, celiac syndrome, habitual vomiting, or other disorders. Hospitalization reverses the infant behavior and restores the mother's confidence in herself to the point that there is no recurrence after discharge from the hospital.

(Presented at the Regional Research Meeting, American Psychiatric Association, Syracuse, N. Y., April 5-6, 1957.)

Organized Enzyme Systems: Mitochondria

Madison, Wis.—Mitochondria as examples of complete enzymatic units containing all the enzymes and cofactors necessary for oxidation, none of which are unrelated, were discussed by David E. Green (Institute for Enzyme Research, University of Wisconsin, Madison). He discussed how these substances are arranged and how they function. The methods employed were those of classic analytic biochemistry and differential centrifugation.

Mitochondria can be prepared in quantities of about 100 Gm. a day from beef heart. By differential centrifugation they can be fragmented into a heavy and a light fraction. Electron microscopy shows the heavy fraction to consist of the mitochondrial cristae (the folded inner portion) and the light fraction to consist of the membranous envelopes surrounding the mitochondria. By chemical analysis the light fraction is found to contain flavin, heme, iron, copper, lipid, and cytochromes A, B, and C_1. The hemes from all three of these cytochromes can be reduced by electrons from either succinate or DPNH.

It is striking that the light mitochondrial fraction prepared from bacteria has the same properties and composition as that from beef heart. Extraction of the light fraction with acetone, under the proper

conditions, yields soluble succinic dehydrogenase, containing 1 molecule of flavin for each 2 of iron. Extraction with 9 per cent alcohol will yield soluble DPNH dehydrogenase with the same proportion of flavin to iron. These two enzymes are present in equal amounts. In the process of oxidation, electrons are taken up by these enzymes (which, of course, are specific for their own substrates). From then on, Dr. Green believes, the electrons are handled by a common pool of cytochromes and other enzymes. Cytochrome A is believed to be the link from cytochromes B and C_1 to molecular oxygen.

Also present in the mitochondrial chain of enzymes are lipid materials, including phospholipids, neutral fats, cholesterols, and a quinone. If this quinone is removed by extraction with heptane, the light fraction is rendered incapable of oxidizing succinate until enzymatic amounts of the quinone are added back. Dr. Green states that cytochrome C_1 can be converted with a lipid. He also expresses the opinion that lipids may compose the "crosslinks" connecting the chains of enzymes in the mitochondria.

Dr. Green plans to analyze other mitochondrial fractions using similar techniques. He hopes eventually to establish all the links in the oxidative chain, which is the basic mechanism for producing energy for all biologic processes.

(Presented as the Eighth Harvey Lecture before the Harvey Society of the New York Academy of Medicine, New York City, April 11, 1957.)

A "Pregnancy" of Five Years' Duration

Rotterdam, The Netherlands.—In 1951 a woman was sent to the hospital when it was found that she was pregnant and the unborn child was dead, reports Rudolf F. v. Wering (Director of School for Midwives, Rotterdam). Since injections of pituitrin had no effect, she was discharged from the hospital after a few days, undelivered. The patient was seen again five years later in a surgical department for a tumor in the abdomen. Roentgenograms disclosed a fetal skeleton. During laparotomy a lithopedion was extracted that lay free between the small bowels; there were no adhesions and no placenta. The patient told the physician that shortly after she left the hospital in 1951, menstruation returned, so that she forgot all about the pregnancy! It is possible that the intensely positive Wassermann reaction gives a better explanation for this forgetfulness, says Dr. Wering.

(Presented at the Joint Meeting of the Netherlands Gynecologic Society and the Belgian Gynecologic Society, Utrecht, The Netherlands, April 13, 1957.)

Progress in the Treatment of Hepatic Coma

Boston.—The current treatment of hepatic coma and its effectiveness at the Boston City Hospital are discussed by Charles Davidson (Associate Professor of Medicine, Harvard University, and Associate Director, Medical Service, Boston City Hospital, Boston). The usual case at this institution is the end result of alcoholic cirrhosis of the liver. The regimen for hepatic coma that has seemed most effective at the Boston City Hospital is as follows: dietary protein withdrawal; administration of oral antibiotics, particularly neomycin; the prompt control of gastrointestinal hemorrhage; the possible use of enema and purge to facilitate removal of protein from the intestinal tract.

With the possible exception of glucose administration, other methods of treatment of hepatic coma recently advocated have not proved valuable. These include the use of glutamate, arginine, and cortisone. Although glutamate and arginine may lower blood ammonia levels, their clinical value has been quite limited. Although ammonia intoxication is probably closely tied in with the clinical manifestations of hepatic coma, there is poor correlation of the arterial or venous ammonia levels with the clinical manifestations of hepatic coma. Furthermore, the rationale for the administration of glutamate and arginine is unclear at the

present time, since their alleviation of the metabolic defects in the citric acid cycle, supposedly caused by ammonia, has not been demonstrated. The intravenous administration of hypertonic saline is occasionally valuable after paracentesis or in overhydrated comatose patients. The cautious use of sedatives and hypnotics is advised. Morphine, paraldehyde, and some barbiturates are poorly handled by the cirrhotic patient Prompt treatment of infection is of value since it occasionally precipitates hepatic coma. Finally, the management of fluid and electrolyte balance is most difficult, requiring careful medical and nursing attention.

(Presented before the New England Medical Center, Boston, March 28, 1957.)

Congenital Abnormalities

London, England.—The physician who tells a mother that her newborn child is perfect is very unwise, says Lindsey W. Batten (General Practitioner, Hampstead, London). It is almost impossible to tell at birth if a child has some congenital abnormality unless it is obvious to the eye. Less than 10 per cent of abnormalities are diagnosed at birth, and many of these 10 per cent, including Mongolism, cretinism, and sexual malformations, are usually readily recognized. Congenital deafness, mental deficiency, blindness, and many cardiac lesions cannot be diagnosed at birth.

Dr. Batten warns against unnecessary exposure of the expectant mother to radiation, which can damage the unborn or even unconceived child. He knows of a young pregnant woman who had 28 diagnostic radiologic examinations of the abdomen and pelvis. How much genetic damage has this done, he asks? Without depriving the individual of his or her liberty, it is impossible to prevent those with defective genes from transmitting them to their unborn children. But physicians can make certain that expectant mothers are not exposed to unnecessary radiation and that young girls are not shielded against rubella, which causes crippling congenital abnormalities if it occurs in the first two months of pregnancy. For this reason, quarantine should not be imposed when local epidemics of the disease occur. In fact, every effort should be made to give girls rubella before marriage, Dr. Batten says. If a pregnant woman is exposed to the risk of this disease, she should be given gamma globulin, he says, and if she should get rubella within the first three months, termination of the pregnancy should be considered. Even if rubel a occurs after the first three months there is still a risk of congenital deafness resulting.

Dr. Batten wonders if other infections might not be responsible for some congenital disease. Pressure effects in utero can produce mechanical defects such as talipes. Dr. Batten says that the eyes of an infant are studied for evidence of sight, but hearing, which may also be defective, is just taken for granted. Deafness is not suspected until a child has reached the age when reaction to sound or speech begins, that is, at about 4 months.

(Presented before the Royal Society of Medicine, Section of General Practice, London, England, March 20, 1957.)

Use of Analgesic Drugs for Relief of Pain

Boston.—There is no satisfactory demonstration in man that analgesic drugs alter the pain threshold in artificially induced pain, declares Henry K. Beecher (Dorr Professor of Anesthesiology, Harvard University Medical School, Boston). If analgesics do not alter this original sensation aspect of pain, they exert their effect on the second phase of pain by altering the reaction or processing phase of pain. This implies not only individual variations but also variations in the circumstances surrounding the pain.

Dr. Beecher cites a study conducted on a series of severely injured soldiers on the Anzio beachhead revealing that 68 per cent of these patients did not want narcotics for relief of pain and 32 per cent did want them. In a similar study of civilians with surgical wounds, 83 per cent did and 17 per cent did

not want narcotics for relief. Dr. Beecher believes that the soldiers realized that they were severely injured and were in pain, but they also realized that for them the war was over and they would soon be going home. He believes this altered their reaction to the pain. The attitude, then, seems important.

The evaluation of analgesics is a difficult one. We must consider not only the relief of pain but the side effects produced as well. In studying relief obtained, Dr. Beecher used patients with severe postoperative pain. They were given drugs by injection and asked at various intervals if half of the pain was gone. Dr. Beecher believes this to have been an adequate criterion and found most patients able to define this well. Double-blind methods and placebos were also used. In studying side effects, the problem is more difficult. Using sick patients is not reliable, since frequently the effects of the disease or injury are not clear-cut from the side effects of the drug. This phase of the studies was carried out in normal healthy adults, although Dr. Beecher admits that this is not an ideal situation. The side effects, other than those visible, such as vomiting or respiratory depression, were recorded by each patient, who was given a check list of a series of adjectives with opposite meaning to answer with each drug given.

Several interesting facts have been obtained from this study. It was found that a 50 mg. dose of meperidine is about equal in pain relief to 10 mg. of morphine. Doubling the dose of meperidine did not significantly increase the number of patients relieved but did greatly increase the side effects. Contrary to earlier reports, meperidine was found to lead to addiction, depress the respiratory center, and not relax all smooth muscle spasm. This is certainly not to imply that meperidine is not a useful drug, but it must be used properly, in proper dosage, for maximal benefit with fewest side effects. Dihydrocodeinone, given in 30 mg. doses, was found to be an excellent agent. At this dosage it has similar pain relief to 10 mg. of morphine, and its side effects are comparable to those of a placebo. Dr. Beecher cautions that the proper dosage, 30 mg., is important if best results are to be obtained.

(Presented before the Anesthesiology Section, Kings County Medical Society, New York City, April 2, 1957.)

Significance of the Rheumatoid Factor

Philadelphia.—The significance of the rheumatoid factor, a substance found in the blood of patients with rheumatoid arthritis, was discussed by a panel of experts, Colin McLeod (Professor of Research Medicine, University of Pennsylvania School of Medicine, Philadelphia) moderating the discussion. Dr. McLeod states that discovery of the rheumatoid factor was the first break in the study of rheumatoid arthritis in years. Occurring in the euglobulin component of rheumatoid serum, it appears with a great deal of consistency in rheumatoid arthritis, rarely in any other diseases. At present, the factor has not been isolated, and many questions remain to be answered: Is it a new product? Is it an increase of a normal component? Is it related to the pathogenesis of rheumatoid arthritis, or is it merely a by-product of the inflammatory process? Is it a true antibody or does it react with immunizing systems by chance? What is its usefulness in the diagnosis and management of rheumatoid arthritis? Dr. McLeod feels that these questions will be well studied in the near future.

(Presented at the Symposium on the Usefulness of Serologic Tests in Rheumatic Diseases, Philadelphia, Feb. 12, 1957.)

BIBLIOGRAPHY

(*Article appears on page 374.*)

1. TISELIUS, A.: A new apparatus for electrophoretic analysis of colloidal mixtures, Tr. Faraday Soc. *33*:524, 1937.
2. SVENSSON, H.: Direkt photographische Aufname von Elektrophorese-Diagrammen, Kolloid Ztschr. *87*:180, 1939.
3. TISELIUS, A.: Zone electrophoresis in filter paper and other media, Tr. Faraday Soc. Discussion no. 13, p. 29, 1953.
4. DURRUM, E. L.: A microelectrophoretic and microionophoretic technique, J. Am. Chem. Soc. *72*:2943, 1950.
5. GRASSMAN, W.; HANNIG, K., AND KNEDEL, M.: Ueber ein Verfahren zur elektrophoretischen Bestimmung der Serum proteine auf Filtrierpapier, Deutsche med. Wchnschr. *76*:333, 1951.
6. KÖIW, E.; WALLENIUS, G., AND GRÖNWALL, A.: Paper electrophoresis in clinical chemistry, Scandinav. J. Clin. & Lab. Invest. *4*:47, 1952.
7. MACKAY, I. R.; VOLWILER, W., AND GOLDSWORTHY, P. D.: Paper electrophoresis of serum proteins: photometric quantitation and comparison with free electrophoresis, J. Clin. Invest. 33:855, 1954.
8. DRABBE, C. A. F., AND REINHOLD, J. G.: Application of zone electrophoresis to analysis of serum proteins, Analyt. Chem. *27*:1090, 1955.
9. KUNKEL, H. G., AND SLATER, R. J.: Lipoprotein patterns of serum obtained by zone electrophoresis, J. Clin. Invest. *31*:677, 1952.
10. KÖIW, E., AND GRÖNWALL, A.: Staining of protein-bound carbohydrates after electrophoresis of serum on filter paper, Scandinav. J. Clin. & Lab. Invest. *4*:244, 1952.
11. LATNER, A., AND UNGLEY, C. C.: Electrophoresis of human gastric juice in relation to Castle's intrinsic factor, Brit. M. J. *1*:467, 1953.
12. MILLS, G. T., AND SMITH, E. E. B.: Electrophoresis of enzymes, Biochem. J. *49*:6, 1951.
13. GORDON, A. H.; GROSS, J.; O'CONNOR, D., AND PITT-RIVERS, R.: Nature of thyroid hormone plasma protein complex, Nature *169*:19, 1952.
14. WALLENIUS, G.: A note on serum iron transportation, Scandinav. J. Clin. & Lab. Invest. *4*:24, 1952.
15. ITANO, H. A.: Clinical states associated with alterations of the hemoglobin molecule, A. M. A. Arch. Int. Med. *96*:287, 1955.
16. REINER, M.; FENICHEL, R. L., AND STERN, K. G.: Electrophoretic studies on protein distribution in normal human serum, Acta haematol. *3*:202, 1950.
17. MOORE, D. H., AND WHITE, J. U.: A new compact electrophoresis apparatus, Rev. Scien. Instruments *19*:700, 1948.
18. LABHART, H., AND STAUB, H.: Mikroelectrophoresis, Helvet. chim. acta *30*:1954, 1947.
19. ANTWEILER, H. J.: Die quantitative Elektrophorese in der Medizin, Berlin, Springer, 1952.
20. STERN, K. G., AND REINER, M.: Electrophoresis in medicine, Yale J. Biol. & Med. *19*:67, 1946.
21. HENLEY, A., AND SCHUETTLER, C. L.: Electrophoresis Bibliography, Silver Spring, Md., American Instrument Co., 1955.
22. GUTMAN, A. B.: The plasma proteins in disease. *In*: ANSON, M. L., AND EDSALL, J. T., EDITORS: Advances in Protein Chemistry, New York, Academic Press, Inc., 1948.
23. LUETSCHER, J. A.: Biological and medical applications of electrophoresis, Physiol. Rev. *27*:621, 1947.
24. FISHER, B.: Recent contributions of electrophoresis to clinical pathology, Am. J. Clin. Path. *23*:246, 1953.
25. ABRAMSON, H. A.; MOYER, L. S., AND GORIN, M. H.: Electrophoresis of Proteins, New York, Reinhold Publishing Corp., 1942.
26. YOUMANS, J. B.: Plasma Proteins, Springfield, Ill., Charles C Thomas, Publisher, 1950.
27. LEWIS, L. A.: Electrophoresis in Physiology, Springfield, Charles C Thomas, Publisher, 1950.
28. BERRY, E. R., AND CHANUTIN, A.: Detailed electrophoretic analysis of sera of healthy young men, J. Clin. Invest. *34*:1513, 1955.
29. GORDON, R. S.: Observations on electrophoretic analysis of normal human serum, Clin. Chem. *2*:31, 1956.
30. DRYER, R. L.; PAUL, W. D., AND ROUTH, J. I.: Effect of acetylsalicylic acid ingestion on electrophoretic patterns of human plasma, Proc. Soc. Exper. Biol. & Med. *66*:552, 1947.
31. COHEN, P. P.; THOMPSON, F. L., AND NITSHE, G. A.: Electrophoretic analysis of ante- and post mortem serum in disease, J. Clin. Invest. *26*:820, 1947.
32. SEIBERT, F. B.; SEIBERT, M. V.; ATNO, A. J., AND CAMPBELL, H. W.: Variation in protein and polysaccharide content of sera in chronic diseases, tuberculosis, sarcoidosis, carcinoma, J. Clin. Invest. *26*:90, 1947.
33. STERLING, K.: The plasma proteins and their abnormalities in disease, Bull. New England M. Center *13*:121, 1951.

34. Bernfeld, P.; Donahue, V. M., and Homburger, F.: Characteristic individual electrophoretic patterns in humans, Proc. Soc. Exper. Biol. & Med. *83*:429, 1953.
35. Rawnsley, H. M.; Yonan, V. L., and Reinhold, J. G.: Serum protein concentrations in the North American Negroid, Science *123*:991, 1956.
36. Lubschez, R.: Electrophoretic patterns in blood plasma and serum in normal children, Pediatrics *2*:570, 1948.
37. Knapp, E. L., and Routh, J. I.: Electrophoretic studies of plasma proteins in normal children, Pediatrics *3*:508, 1949.
38. Schar, E.; Bossak, E. T.; Wang, C., and Adlersberg, D.: Serum components in the newborn, Science *123*:461, 1956.
39. Rafsky, H. A.; Brill, A. A.; Stern, K. G., and Corey, H.: Electrophoretic studies on serum of normal aged individuals, Am. J. M. Sc. *224*:522, 1952.
40. Coryell, M. N.; Beach, E. F.; Robinson, A. R.; Macy, I. G., and Mack, H. C.: Metabolism of women during the reproductive cycle, J. Clin. Invest. *29*:1559, 1950.
41. Macy, I. G., and Mack, H. C.: Physiological Changes in Plasma Proteins Characteristic of Human Reproduction, Detroit, Children's Fund of Michigan, 1952.
42. Mack, H. C.; Robinson, A. R.; Wiseman, M. E.; Schoeb, E. J., and Macy, I. G.: Plasma proteins in toxemias of pregnancy, J. Clin. Invest. *30*:609, 1951.
43. Mack, H. C.; Thostison, G.; Wiseman, M. E.; Robinson, A. R., and Moyer, E. Z.: Pregnancy complicated by diabetes mellitus, Obst. & Gynec. *1*:74, 1953.
44. Parviainen, S.; Soiva, K., and Ehrnrooth, C. A.: Electrophoretic study of proteinuria in toxemia of late pregnancy, Scandinav. J. Clin. & Lab. Invest. *3*:282, 1951.
45. Taylor, H. L.; Mickelsen, O., and Keys, A.: Effects of induced malaria, acute and semi-starvation on the serum proteins of normal young men, J. Clin. Invest. *28*:273, 1949.
46. Elman, R.: Clinical problems in hypoproteinemia due to protein deprivation. *In:* Youmans, J. B., editor: Plasma Proteins, Springfield, Ill., Charles C Thomas, Publisher, 1950.
47. Hoch-Ligeti, C.; Irvine, K., and Sprinkle, E. P.: Investigation of serum protein patterns in patients undergoing operation, Proc. Soc. Exper. Biol. & Med. *84*:707, 1953.
48. Prendergast, J. J., and Fenichel, R. L.: Electrophoretic and electrolytic changes in blood, J. Michigan M. Soc. *53*:1336, 1954.
49. Williamson, M. B.: Protein metabolism during healing of wounds, Clin. Chem. 2:1, 1956.
50. Rottino, A.; Suchoff, D., and Stern, K. G.: Electrophoretic study of blood serum from lymphogranulomatous patients, J. Lab. & Clin. Med. *33*:624, 1948.
51. Petermann, M. L.; Karnofsky, D. A., and Hogness, K. R.: Electrophoretic studies on plasma of patients with neoplastic disease, Cancer *1*:109, 1948.
52. Young, E. G., and Webber, R. V.: Electrophoretic analyses in selected pathological states, Canad. J. M. Sc. *31*:45, 1953.
53. Arends, T.; Coonrad, E. V., and Rundles, R. W.: Serum proteins in Hodgkin's disease and malignant lymphoma, Am. J. Med. *16*:833, 1954.
54. Wilson, M. G., and Lubschez, R.: Electrophoretic patterns of blood plasma and serum in rheumatic children, Pediatrics *2*:570, 1948.
55. Jackson, R. L.; Kelly, H. G.; Smith, E. K.; Wang, P., and Routh, J. I.: Electrophoretic analysis of plasma of rheumatic fever patients in relation to stages of disease, A. M. A. Am. J. Dis. Child. *86*:403, 1953.
56. Hunt, T. E., and Trew, J. A.: Zone electrophoretic studies of plasma proteins in rheumatoid arthritis and ankylosing spondylitis, Ann. Rheumat. Dis. *13*:201, 1954.
57. Routh, J. I., and Paul, W. D.: Electrophoretic analyses of plasma and serum proteins in rheumatoid arthritis, Arch. Phys. Med. *31*:511, 1950.
58. Laurell, H.: Demonstration of two new electrophoretic components in a serum from a patient with rheumatoid arthritis, Arkiv. Kemi *3*:115, 1951.
59. Reid, A. F.; Pike, R. M.; Sulkin, S. E., and Coggeshall, H. C.: Electrophoretic characterization of serum from rheumatoid arthritis patients, J. Lab. & Clin. Med. *37*:264, 1951.
60. Perlmann, G. E.; Ropes, M. W.; Kaufman, D., and Bauer, W.: The electrophoretic patterns of proteins in synovial fluid and serum in rheumatoid arthritis, J. Clin. Invest. *33*:319, 1954.
61. Gaebler, O. H.; Beher, W. T.; Sigler, J. W., and Galpin, R. R.: Reproducibility and validity of sodium sulfate fractionation of proteins in plasma and knee-joint fluid, Clin. Chem. *1*:105, 1955.
62. Reiner, M.: Effect of cortisone and ACTH therapy on serum proteins in dis. lupus erythematosus, Proc. Soc. Exper. Biol. & Med. *74*:529, 1950.
63. Mahaux, J.; Denolin-Reubens, R., and Mascart, P.: Les caractères biologiques du lupus érythémateux aigu dis., Rev. d'hémat. *8*:77, 1953.
64. Sonne, L. M., and Schwartz, M.: Lupus erythematosus disseminatus, Acta dermat.-venereol. *32*:333, 1952.
65. Govaerts, P.; Herlant, M.; Mahaux, J.; Toussaint, C.; Van der Meiren, L., and Brihaye-van Geertruyden, M.: Etude clinique, histologique, et histochimique d'un cas de lupus érythémateux aigu disseminé, Acta clin. belg. *8*:385, 1953.
66. Boas, N. F., and Reiner, M.: Effect of ACTH and cortisone on serum hexosamine and gamma globulin levels in acute dis. lupus erythematosus, J. Clin. Endocrinol. *11*:890, 1951.

67. Haserick, J. R.; Lewis, L. A., and Bortz, D. W.: Blood factor in acute dis. lupus erythematosus. I. Determination of gamma globulin as a specific plasma fraction, Am. J. M. Sc. *219*:660, 1950.
68. Sayers, G.; Burns, T. W.; Tyler, F. H.; Jager, B. V.; Schwartz, T. B.; Smith, E. L.; Samuels, L. T., and Davenport, H. W.: Metabolic actions and fate of intravenously administered adrenocorticotropic hormone in man, J. Clin. Endocrinol. *9*:593, 1949.
69. Jager, B. V.; Brown, H., and Nickerson, M.: Alterations in plasma proteins, plasma volume, red blood cells in patients receiving ACTH or cortisone, J. Lab. & Clin. Med. *37*:431, 1951.
70. Paul, W. D.; Hodges, R. E.; Bean, W. B.; Routh, J. I., and Daum, K.: Effects of nitrogen mustard therapy in patients with rheumatoid arthritis, Arch. Phys. Med. *35*:371, 1954.
71. Dryer, R. L.; Paul, W. D., and Routh, J. I.: Effect of acetylsalicylic acid ingestion on electrophoretic patterns of human plasma, Proc. Soc. Exper. Biol. & Med. *66*:552, 1947.
72. Walker, S. A., and Benditt, E. P.: The serum proteins in diseases of connective tissue, J. Invest. Dermat. *14*:113, 1950.
73. Pearsall, H. E., and Chanutin, A.: Electrophoretic, nitrogen and lipid analysis of plasma and fractions in disease, Am. J. Med. *7*:301, 1949.
74. Donzelot, E.; Kaufmann, H., and de Mende, S.: Resultats de l'electrophorèse dans les affections cardio-vasculaires, Presse méd. *57*:701, 1949.
75. Ortiz-Vázquez, J.; Alvarez, J. G., and Otero, J. L. G.: Las proteínas séricas en la insuficiencia cardíaca congestiva: estudio electroforético de 25 casos, Rev. clín. espan. *52*:24, 1954.
76. Adlersberg, D.; Bossak, E. T.; Sher, I. H., and Sobotka, H.: Electrophoresis and monomolecular layer studies with serum lipoproteins, Clin. Chem. *1*:18, 1955.
77. Atlas, D. H.; Goldfarb, A. R., and Gaberman, P.: Electrophoresis in hypothyroidism, Proc. Soc. Exper. Biol. & Med. *74*:653, 1950.
78. Mustacchi, P.; Petermann, M. L., and Rall, J. E.: Changes in human plasma mucoproteins in hyperthyroidism and myxedema, J. Lab. Endocrinol. & Metab. *14*:729, 1954.
79. Mahaux, J., and Köiw, E.: Le proteinogramme et le lipoidgramme sur papier filtre dans le myxoedeme, Ann. d'endocrinol. *13*:691, 1952.
80. Lewis, L. A., and McCullagh, E. P.: Plasma protein pattern in Cushing's syndrome, J. Clin. Endocrinol. *7*:559, 1947.
81. McCullagh, E. P., and Lewis, L. A.: Tiselius electrophoresis studies of plasma proteins in Addison's disease, Am. J. M. Sc. *210*:81, 1945.
82. Routh, J. I.; Knapp, E. L., and Kobayashi, C. K.: Electrophoretic studies of plasma and urinary proteins in children with lipoid nephrosis, J. Pediat. *33*:688, 1948.
83. Fischer, M. A.; Steinman, P. A.; Carpenter, A. M., and Menten, M. L.: Qualitative and quantitative changes in the plasma proteins of lipoid nephrosis, J. Lab. & Clin. Med. *37*:894, 1951.
84. Mehl, J.: Electrophoretic studies of the plasma protein changes in neoplastic diseases, Texas Rep. Biol. & Med. *8*:169, 1950.
85. Soshea, J. W., and Farnsworth, E. B.: Serum lipid analysis in the nephrotic syndrome under ACTH administration, J. Lab. & Clin. Med. *38*:414, 1951.
86. Farnsworth, E. B., and Ruppenthal, N. C.: Electrophoretic studies on serum and urine proteins in nephrosis treated with ACTH, J. Lab. & Clin. Med. *38*:407, 1951.
87. Rafsky, H. A.; Weingarten, M.; Krieger, C. I.; Stern, K. G., and Newman, B.: Electrophoretic studies in liver disease, Gastroenterology *14*:29, 1950.
88. Saifer, A.: Protein flocculation reactions, Am. J. Med. *13*:730, 1952.
89. Wunderly, C., and Wuhrmann, F.: The effect of experimental increases in the gamma globulin and albumin content of sera on the response given by turbidity and flocculation tests, Brit. J. Exper. Path. *28*:286, 1947.
90. Wuhrmann, F., and Wunderly, C.: Die Bluteiweisskörper des Menschen, Basel, B. Schwabe & Co., 1952.
91. Popper, H.; Huerga, J. de la; Steigmann, F., and Slodki, M.: Turbidimetric gamma globulin determinations in hepatobiliary diseases, J. Lab. & Clin. Med. *35*:391, 1950.
92. Reinhold, J. G.: Chemical evaluation of the functions of the liver, Clin. Chem. *1*:351, 1955.
93. Mandel, E. E.; Gorsuch, T. L., and Cooper, G. E.: Seromucoid in hepatobiliary disease, Clin. Chem. *1*:221, 1955.
94. Martin, N. H.: Interrelations of serum proteins in liver damage with special reference to the thymol test, J. Clin. Path. *2*:275, 1949.
95. Viollier, G.: Biochimie des lésions experimentales et cliniques due foie, Helvet. med. acta *17*:354, 1950.
96. Popper, H.; Bean, W. B.; Huerga, J. de la; Franklin, M.; Tsumagari, Y.; Routh, J. I., and Steigmann, F.: Electrophoretic serum protein fractions in hepatobiliary disease, Gastroenterology *17*:138, 1951.
97. Sherlock, S., and Wolstenholme, G. E. W.: Liver Disease, Philadelphia, Blakiston Co., 1951.
98. Hanger, F. M.: Abnormalities in the globulin component of serum by the cephalin-flocculation test, Tr. A. Am. Physicians *60*:82, 1947.
99. MacLagan, N. F.: Flocculation tests: chemical and clinical significance, Brit. M. J. *2*:892, 1948.
100. Kunkel, H. G.: Estimation of alteration of serum gamma globulin by turbidimetric technique, Proc. Soc. Exper. Biol. & Med. *66*:217, 1947.

101. Katz, E. J.; Hasterlik, R. J., and Snapp, F. E.: Studies of the thymol turbidity, cephalin flocculation and thymol flocculation tests, J. Lab. & Clin. Med. *44*:353, 1954.
102. Spellberg, M. A.; Cohn, C.; Wolfson, W. Q., and Shore, C.: Serum globulin fractions as an index of hepatic dysfunction, Gastroenterology *14*:11, 1950.
103. Maher, F. T.; Snell, A. M., and Mann, F. D.: Turbidimetric estimation of serum colloids in the differential diagnosis of hepatobiliary disease, Gastroenterology *12*:394, 1949.
104. Hartmann, F.: Untersuchungen ueber die Beurteilung der Funktion der Leber auf Grund von Störungen ihrer Stoffwechselleistungen: Beurteilung der Leberfunktion durch Untersuchungen des Eiweissstoffwechsels, Z. klin. Med. *147*:375, 1950.
105. Huerga, J. de la; Popper, H.; Franklin, M., and Routh, J. I.: Comparison of the results of gamma globulin and zinc sulfate turbidity tests with electrophoretic determination of gamma globulins, J. Lab. & Clin. Med. *35*:466, 1950.
106. Kibrick, A. C., and Clements, A. B.: A comparative study of the serum albumin-globulin ratio, the cephalin-cholesterol flocculation and the thymol turbidity tests for liver function, J. Lab. & Clin. Med. *33*:662, 1948.
107. Strade, H. A.; Dotti, L. B., and Ilka, S. J.: A clinical evaluation of the colloidal red test in comparison with the thymol turbidity test, Am. J. M. Sc. *217*:448, 1949.
108. Volk, B. W.; Saifer, A.; Johnson, L. E., and Oreskes, I.: Electrophoretic and chemical serum protein fractions in pulmonary tuberculosis, Am. Rev. Tubercu. *67*:299, 1953.
109. Levin, B. M.; Kaufman, H., and Huerga, J. de la: Gamma globulin studies in tuberculosis in children, A. M. A. Am. J. Dis. Child. *83*:26, 1952.
110. Routh, J. I., and Paul, W. D.: Electrophoretic studies of plasma and serum proteins in ant. poliomyelitis, Arch. Phys. Med. *32*:397, 1951.
111. Steigmann, A. J.; Brodsky, W. A., and Stephens, R. N.: Normal distribution of serum protein levels in acute poliomyelitis patients, J. Lab. & Clin. Med. *39*:757, 1952.
112. Benditt, E. P., and Walker, S. A.: Serum proteins in syphilis, Am. J. Med. *4*:663, 1948.
113. Sterling, K.: Serum proteins in infectious mononucleosis, J. Clin. Invest. *28*:1057, 1949.
114. Benhamou, E.: Les protéines sériques dans les Maladies Infectieuses, Ann. méd. *48*:225, 1947.
115. Waldenström, J.; Pedersen, K. O.; Harboe, N., and Sonck, C. E.: Ultracentrifugation, electrophoresis and viscometry of serum proteins. I. Lymphogranuloma venereum, Acta med. Scandinav. *141*:195, 1951.
116. Reiner, M.: Application of electrophoresis to medical problems, M. Ann. District of Columbia *21*:11, 1952.
117. Chakravarti, H.: Studies on plasma protein, Indian M. Gaz. *85*:141, 1950.
118. Most, H., and Lavietes, P. H.: Kala-azar in military personnel, Medicine *26*:221, 1947.
119. Cooper, G. R.; Rein, C. R., and Beard, J. W.: Electrophoretic analysis of Kala-azar human serum, Proc. Soc. Exper. Biol. & Med. *61*:179, 1946.
120. Bruton, O. C.: Agammaglobulinemia, Pediatrics *9*:722, 1952.
121. Martin, C. M.; Gordon, R. S., and McCullough, N. B.: Acquired hypogammaglobulinemia in an adult, New England J. Med. *254*:449, 1956.
122. Wyngaarden, J. B.; Crawford, J. D.; Chamberlin, H. R., and Lever, W. F.: Idiopathic hypoproteinemia, Pediatrics *9*:729, 1952.
123. Schick, B., and Greenbaum, J. W.: Edema with hypoproteinemia due to a congenital defect in protein formation, J. Pediat. *27*:241, 1945.
124. Bendich, A., and Kabat, E. A.: Immunochemical estimation of the rate of disappearance of transfused gamma globulin from the blood in two cases of hypoproteinemia, J. Lab. & Clin. Med. *34*:1066, 1949.
125. Lever, W. F.; Schultz, E. L., and Hurley, N. A.: Plasma proteins in various diseases of the skin, A. M. A. Arch. Dermat. & Syph. *63*:702, 1951.
126. Walker, S. A., and Benditt, E. P.: An electrophoretic study of the serum proteins in scleroderma, Proc. Soc. Exper. Biol. & Med. *67*:504, 1948.
127. Lever, W. F.: Proteins in pemphigus vulgaris, J. Invest. Dermat. *14*:205, 1950.
128. Sherman, W. B., and Seebohm, P. M.: Passive transfer of cold urticaria, J. Allergy *21*:414, 1950.
129. Campbell, D. H.; Cann, J. R.; Friedman, T. B., and Brown, R. A.: Reagic serum fractions obtained by the electrophoresis convection method, J. Allergy *21*:519, 1950.
130. Seibert, F. B., and Nelson, Y. H.: Electrophoretic identification of antibody to tuberculin protein, Proc. Soc. Exper. Biol. & Med. *49*:77, 1942.
131. Cooke, R. A.; Sherman, W. B.; Menzel, A. E. O.; Chapin, H. B.; Howell, C. M.; Scott, R. B.; Myers, P. A., and Downing, L. M.: ACTH and cortisone in allergic diseases, J. Allergy 22:211, 1951.
132. Cann, J. R.; Brown, R. A.; Kirkwood, J. G.; Sturgeon, P., and Clarke, D. W.: Studies of antibody distribution in the serum proteins of several Rh antisera, J. Immunol. *68*:243, 1952.
133. Saifer, A.; Rabiner, A. M.; Oreskes, I., and Volk, B. W.: Electrophoretic and chemical serum protein fractions in multiple sclerosis, Am. J. M. Sc. *225*:287, 1953.
134. Bernsohn, J., and Cochrane, L. S.: Electrophoretic fractionation of serum proteins in multiple sclerosis, Proc. Soc. Exper. Biol. & Med. *86*:540, 1954.

135. Kabat, E. A.; Freedman, D. A.; Murray, J. P., and Knaub, V.: A study of the crystalline albumin, gamma globulin and total protein in spinal fluid of 100 cases of multiple sclerosis, Am. J. M. Sc. *219*:55, 1950.
136. Roboz, E.; Murphy, J. B.; Hess, W. C., and Forster, F. M.: Isolation and determination of the glycoproteins in cerebrospinal fluid, Proc. Soc. Exper. Biol. & Med. *89*:691, 1955.
137. Ewerbeck, H.: Die elektrophoretische Darstellung Normalen Menschlichen Liquors, Klin. Wchnschr. *28*:692, 1950.
138. Cummings, J. N.: The examination of cerebrospinal fluid and cerebral cyst fluid by paper strip electrophoresis, J. Neurol., Neurosurg. & Psychiat. *16*:152, 1952.
139. Eaton, J. C., and Gardner, M. D.: Separation of cerebrospinal fluid proteins by paper electrophoresis, Biochem. J. *55*:25, 1953.
140. Bucher, T.; Metzelt, D., and Pette, D.: Papier Elektrophorese von Liquor Cerebrospinales, Klin. Wchnschr. *30*:325, 1952.
141. Schneider, G., and Wallenius, G.: Electrophoretic studies on cerebrospinal fluid proteins, Scandinav. J. Clin. & Lab. Invest. *3*:145, 1951.
142. Hoch, H., and Chanutin, A.: Electrophoretic studies on cerebrospinal fluid, Proc. Soc. Exper. Biol. & Med. *81*:628, 1952.
143. Aly, F. W.: Untersuchungen ueber die elektrophoretische isolierte Vorfraktion aus Liquor cerebrospinalis, Biochem. Ztschr. *325*:505, 1954.
144. Bauer, H.: Ueber die Bedeutung der Papier-Elektrophorese des Liquors für die klinische Forschung, Deut. Z. Nervenheilk. *170*:381, 1953.
145. Caspani, R., and Sticca: L'analisi elletroforetica delle proteine liquorali nelle miningiti e miningonervassiti acute non purulente, Minerva med. 2:749, 1952.
146. Paulino, L.; Itano, H. A.; Singer, S. J., and Wells, I. C.: Sickle cell anemia, a molecular disease, Science *110*:543, 1949.
147. Itano, H. A.: Human hemoglobin, Science *117*:89, 1953.
148. Thorup, O. A.; Itano, H. A.; Wheby, M., and Leavell, B.: Hemoglobin, Science *123*:889, 1956.
149. Fenichel, R. L.; Watson, J., and Eirich, F.: Electrophoretic studies of the plasma and serum proteins in sickle cell anemia, J. Clin. Invest. *29*:1620, 1950.
150. McIlvanie, S. K., and Beard, M. F.: Paroxysmal nocturnal hemoglobinuria, Blood *6*:936, 1951.
151. Simpson, N. H., and Oldham, E. C.: Chronic hemolytic anemia with paroxysmal nocturnal hemoglobinuria, Am. J. Med. *9*:414, 1950.
152. Bernfeld, P.; Stefanini, M.; Berkowitz, R. D., and Hennessey, F. B.: Electrophoretic plasma protein patterns in families with hemophilia, Proc. Soc. Exper. Biol. & Med. *83*:311, 1953.
153. Reiner, M., and Stern, K. G.: Electrophoretic studies on the protein distribution in the serum of multiple myeloma patients, Acta hematol. *9*:19, 1953.
154. Snapper, I.; Turner, L. B., and Moscovitz, H. L.: Multiple Myeloma, New York, Grune & Stratton, 1953.
155. Putnam, F. W., and Miyake, A.: On the non-identity of Bence-Jones proteins, Science *120*:848, 1954.
156. Hardy, S., and Putnam, F. W.: Proteins in multiple myeloma. III. Origin of Bence-Jones protein, J. Biol. Chem. *212*:361, 1955.
157. Hardy, S., and Putnam, F. W.: Proteins in multiple myeloma. IV. Interaction with metabolic nitrogen, J. Biol. Chem. *212*:371, 1955.
158. Stern, K. G., and Laszlo, D.: Protein and metabolic studies in multiple myeloma, Cancer Research *10*:242, 1950.
159. Korngold, L., and Lipari, R.: Multiple myeloma proteins. I. Immunological studies, Cancer *9*:183, 1956.
160. Block, W. D.; Rukavina, J. G., and Curtis, A. C.: An atypical electrophoretic peak in serum of patients with familial primary systemic amyloidosis, Proc. Soc. Exper. Biol. & Med. *89*:175, 1955.

health and travel

Complete proceedings of the First Symposium on Health and Travel, held in June of 1955. Travel for the young, the old, the sick; by car, air, train, boat, and space ship; in the continental U. S., Europe, Latin America, Asia; in tropical and subtropical climes. All these problems are covered in their physiologic and psychologic aspects by top specialists in their field. The monograph includes detailed information on prophylaxis and treatment, as well as historical and entertaining general data. This attractive hard-cover book is a classic reference book for your library, as well as an attractive and much appreciated gift for a fellow physician. 72 pp. **Price: $3.00.**

contents

THE PHYSICIAN AS TRAVELER
by Féliz Martí-Ibáñez, M.D.,
Editor-in-Chief, INTERNATIONAL RECORD OF MEDICINE & GENERAL PRACTICE CLINICS.

WHEN CHILDREN TRAVEL
by I. Newton Kugelmass, M.D.,
Consultant, Dept. of Health & Hospitals, New York City.

WHEN PEOPLE WHO ARE NOT YOUNG TRAVEL
by William T. Foley, M.D.,
Assistant Professor of Clinical Medicine & Chief of the Vascular Clinics, New York Hospital, New York City.

INFECTIONS AND TRAVEL
by Elmer H. Loughlin, M.D.,
Associate Clinical Professor of Medicine, New York Medical College, Flower & Fifth Avenue Hospital, New York City.

WHEN SICK PEOPLE TRAVEL
by Walter C. Alvarez, M.D.,
Editor-in-Chief, MODERN MEDICINE

TRAVEL AND MOTION SICKNESS
by Herman I. Chinn, Ph.D.,
Chief, Dept. of Pharmacology-Biochemistry, USAF School of Aviation, Randolph Field, Texas.

STRESS AND TRAVEL
by Gaétan Jasmin, M.D.,
Institute of Experimental Medicine, Montreal, Canada.

SEA TRAVEL AND HEALTH
by William L. Wheeler, Jr., M.D.,
Medical Director, W. R. Grace & Company, New York City.

GEOGRAPHY, TRAVEL AND DISEASE
by Jacques, M. May
Head, Dept. of Medical Geography, American Geographical Society, New York City.

MEDICAL PROBLEMS OF SPACE FLIGHT
by Hubertus Strughold, M.D,
Chief, Dept. of Space Medicine, USAF School of Aviation Medicine, Randolph Field, Texas.

PHYSIOLOGIC DAY-NIGHT CYCLE AFTER LONG DISTANCE FLIGHTS
by Hubertus Strughold, M.D., Ph.D.,
Chief, Dept. of Space Medicine, USAF School of Aviation Medicine, Randolph Field, Texas.

NUTRITION AND FLIGHT
by Col. Miriam E. Perry,
Chief, Women's Medical Specialist Corps, USAF, Office of Surgeon General, Washington, D. C.

NEW PERSPECTIVES OF HEALTH AND TRAVEL. A SUMMATION OF THE SYMPOSIUM
by Féliz Martí-Ibáñez, M.D.,
Editor-in-Chief of the INTERNATIONAL RECORD OF MEDICINE & GENERAL PRACTICE CLINICS.

WRITE TO: MD PUBLICATIONS, INC., 30 EAST 60TH STREET, NEW YORK 22, N. Y.

A new, essential, and timely book

ANTIBIOTICS ANNUAL 1956-1957

Edited by Henry Welch, Ph.D., and Félix Martí-Ibáñez, M.D.

Proceedings of the Fourth Annual Symposium on Antibiotics.
Washington, D. C., October 17, 18, and 19, 1956

155 REPORTS ON THE LATEST FINDINGS IN ANTIBIOTICS

by

390 AUTHORS REPRESENTING 12 COUNTRIES

Panel Discussions

- Antibiotics in Intestinal Antisepsis—Edwin J. Pulaski, Moderator
- Susceptibility of Microorganisms to Antibiotics Isolated from Hospitalized and Nonhospitalized Persons—W. A. Altemeier, Moderator
- Present Status of Antibiotics in the Preservation of Food—W. B. Rankin, Moderator

Some Selected Subjects Among the 155 Papers

- Further reports on the new antibiotic oleandomycin
- New novobiocin preparations
- The value of antibiotic combinations
- Complete descriptions of research on 4 new antibiotics: ristocetin, nucleocidin, elazocepdin, and PA 132
- A comparison of various antibiotic agents in pre- and postoperative therapy
- Continued clinical studies on vancomycin
- Latest uses of antibiotics in the preservation of foods
- The local management of burns
- The problems of synergism and resistance
- Newest indications for erythromycin therapy

A Unique and Indispensable Volume for Every Physician, Research Worker, and Teacher

ONLY $10.00 for a copy of this attractive, hardbound volume of over 1000 pages in length, including charts, illustrations, and a comprehensive index.

MEDICAL ENCYCLOPEDIA, INC.
20 East 60th Street, New York 22, N. Y.

Please send me one copy of **ANTIBIOTICS ANNUAL 1956-1957** at only $10.00 a copy.

☐ Check enclosed. ☐ Bill me.

Name .....
(Please print plainly)

Address .....

City ..... *Zone* ..... *State* .....